Self-Assembly of Janus Type Amphiphilic Dendrimers from Dissipative Particle Dynamics Simulation

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Abstract—The self-assembly of Janus type amphiphilic dendrimers has been studied extensively through experiments and computer simulations, while most of the simulations assume that Janus molecules are connected by covalent bonds, disregarding the noncovalent interaction which evokes the particular dynamic self-assembly regulation. This paper investigates the dynamic self-assembly behavior of Janus type amphiphilic dendrimers through the dissipative particle dynamics (DPD) method. A series of coarse-grained models of Janus type amphiphilic dendrimers with different hydrophobic-hydrophilic ratios were constructed to simulate the static self-assembly, and then the dynamic self-assembly was carried out through introducing a chemical bonding reaction to simulate the non-covalent interaction between the two different parts of Janus type dendrimers. The control of reaction rate was accomplished by modifying the reaction probability to adjust the dynamic self-assembly process. The results indicate that the introduction of non-covalent interaction changes the self-assembly behavior of some models and generates different dynamic self-assembly structures. It can also be deduced that the reaction rate exerts influence on the structure of dynamic self-assembly.

1. INTRODUCTION
Janus type amphiphilic dendrimers are one of the popular candidates for the building units of supramolecular systems and the models of corresponding simulation systems since their structures, sizes and internal functional groups can be precisely controlled. Due to the unique molecular structures and self-assembly behaviors, a series of self-assembly structures of Janus type amphiphilic dendrimers with different morphologies have been obtained, such as vesicles [1], rods, dish-like structures and Toroidal structures [2].

Although the majority of researches on the self-assembly behaviors of Janus particles have been conducted through Monte Carlo (MC) and Molecular Dynamics (MD) methods [1-3], both MC and MD methods are confronted with some drawbacks during the simulation of the self-assembly behavior of Janus-type amphiphilic molecules: MC method cannot expound the kinetic process of self-assembly, and the size of the system that MD method can simulate is limited. It is difficult to eliminate the influence of the finite size effect while using MD method, and the time required for the simulation system to reach equilibrium is relatively long.

Compared with MC and MD methods, the dissipative particle dynamics simulation (DPD) method can not only present the kinetic processes, but also support simulations with longer time and larger space scale [4], which is very suitable for the study of the self-assembly behavior of dendrimers. This research utilizes the DPD simulation method to study the dynamic self-assembly behavior of Janus-type amphiphilic dendrimers. By constructing and adjusting the reversible reaction system and changing the ratio of hydrophilic and hydrophobic dendrimers, the dynamic self-assembly mechanism of Janus type amphiphilic dendrimers and the relationship between assembly structure and dynamic reaction rate are revealed.
2. Method

2.1 Calculation Principle

Dissipative Particle Dynamics (DPD) is a mesoscopic computer simulation method developed by Hoogerbrugge and Koelman [5,6] in the early 1990s. In the DPD model [7], a particle represents a collection of many molecules. The motion of all interacting particles follows the Newtonian motion equation:

\[
\frac{d\vec{r}_i}{dt} = \vec{v}_i \tag{1}
\]

\[
\frac{d\vec{v}_i}{dt} = \sum_{j\neq i} (\vec{F}^C_{ij} + \vec{F}^D_{ij} + \vec{F}^R_{ij}) = \vec{F}_i \tag{2}
\]

\(\vec{r}_i\) and \(\vec{v}_i\) are the position and velocity vectors of the particles, respectively. To simplify the calculation, the mass of all particles in the DPD model is set to 1, so the total force which each particle receives is equal to its acceleration. The total force consists of three parts: conservative force \(\vec{F}^C_{ij}\), dissipation force \(\vec{F}^D_{ij}\) and random force \(\vec{F}^R_{ij}\), which are all pair-wise interaction forces. The scope of action of all these forces is within a certain cutoff radius \(r_C\), which is generally set as a unit length in the DPD model (\(r_C=1\)). The conservative force is a force acting in the direction of the line connecting the centroids of the paired particles, and is inversely proportional to the distance between the pair of particles:

\[
\vec{F}^C_{ij} = \alpha_{ij} (1 - r_{ij}) \vec{e}_{ij} \tag{3}
\]

\(\alpha_{ij}\) is the maximum repulsive force between particles \(i\) and \(j\), \(r_{ij} = r_j - r_i, r_{ij} = |\vec{r}_i - \vec{r}_j| / r_j\). Moreover, the action forms of dissipative force and random force are:

\[
\vec{F}^D_{ij} = -\gamma \omega^D (r_{ij})(\vec{e}_{ij} \cdot \vec{v}_i) \vec{v}_j \tag{4}
\]

\[
\vec{F}^R_{ij} = \sigma \omega^R (r_{ij}) \theta_{ij} \vec{\xi}_{ij} \tag{5}
\]

\(\omega^D\) and \(\omega^R\) are two weighting functions that depend on the relative distance between particles. They describe the attenuation of dissipative force and random force as the distance between particles increases. \(\vec{v}_i = \vec{v}_j - \vec{v}_j\), \(\theta_{ij}\) is a random number with Gaussian distribution and unit variance: \(\langle \theta_{ij} (t) \rangle = 0\), \(\langle \theta_{ij} (t) \theta_{ij} (t') \rangle = (\delta_{tt'} + \delta_{ij} \delta_{jj'}) \delta (t - t')\), this relation ensures that the random forces received by different interacting particles at different moments are independent of each other, and its symmetry relation \(\theta_{ij} = \theta_{ji}\) ensures the momentum conservation of the system. During the simulation, a random number sequence uniformly distributed between 0 and 1 is invoked. For each pair of interacting particles at each moment, a different random number \(u\) is \(r\) generated, and then the Gaussian random number above \(\theta_{ij}\) is replaced by \(\xi_{ij} = \sqrt{3(2u - 1)}\). Such method of generating random numbers is very effective, and the numbers are no different from the ones obtained by Gaussian random number generator [8]. The two coefficients \(\gamma\) and \(\sigma\) are used to describe the magnitude of the dissipation force and random force, respectively. The dissipation force represents the friction between particles, which is proportional to the relative speed between the interacting particle pairs, consuming the energy of the system. The action of random force compensates for the decrease of system’s degree of freedom (DOF), which is caused by the coarse-graining, and acts as a heat source to supplement energy for the system.

When the DPD model is applied to a polymer system, it is necessary to consider the spring force
connecting adjacent particles. \( \vec{F}_v = k(r_v - r_{eq})\vec{v}_v \), \( k \) is the spring constant, \( r_{eq} \) is the equilibrium length of the spring, and this force should also be considered as a part of the conservative force. In this research, \( k=4.0, r_{eq}=0 \).

Espanol and Warren [9] proposed in 1995 that the weight functions of the dissipation force and the random force can be selected arbitrarily, but the following relation must be satisfied:

\[
\omega^\alpha(\vec{r}_i) = \omega^\beta(\vec{r}_i)^2
\]

\[
\sigma^2 = 2\gamma k_T T
\]

Normally \( \gamma=4.5 \), and according to the reference, \( \omega^\alpha \) and \( \omega^\beta \) conform to the following relation:

\[
\omega^\alpha(\vec{r}_i) = [\omega^\beta(\vec{r}_i)]^2 = (1 - r_{eq})^2
\]

Compared with the velocity-Verlet in molecular dynamics simulation, the original DPD-velocity-Verlet (DPD-VV) algorithm considered the dependence of the dissipation force on the velocity, but did not introduce any adjustment parameters. In 1997, Groot and Warren [10] modified the method, and the integration process was as follows:

\[
\vec{v}_i \leftarrow \vec{v}_i + \frac{1}{2m} (\vec{F}_i^C \delta t + \vec{F}_i^D \delta t + \vec{F}_i^R \sqrt{\delta t})
\]

\[
\vec{v}^\alpha_i \leftarrow \vec{v}_i + \lambda \frac{1}{m} (\vec{F}_i^C \delta t + \vec{F}_i^D \delta t + \vec{F}_i^R \sqrt{\delta t})
\]

\[
\vec{r}_i \leftarrow \vec{r}_i + \vec{v}_i \delta t
\]

Calculate \( \vec{F}_i^C(\vec{r}), \vec{F}_i^D(\vec{r}, \vec{v}^\alpha_i), \vec{F}_i^R(\vec{r}) \)

\[
\vec{v}_i \leftarrow \vec{v}_i + \frac{1}{2m} (\vec{F}_i^C \delta t + \vec{F}_i^D \delta t + \vec{F}_i^R \sqrt{\delta t})
\]

The main feature of this method is the introduction of an adjustable parameter \( \lambda \) during the integration process. \( \lambda \) is used to predict a new particle velocity \( \vec{v}_i^\alpha \), then \( \vec{v}_i^\alpha \) is used to calculate the force, and finally update the real velocity \( \vec{v}_i \). The parameter \( \lambda \) is generally selected as 0.65.

2.2 Model Establishment

This research is devoted to build a universal model for the amphiphilic dendrimers and explore their self-assembly process. Through the DPD method, a coarse-grained model \( A_xB_y \) is constructed, which \( A \) and \( B \) represent the hydrophilic particles and hydrophobic particles respectively. They do not correspond to any certain atoms, but represent collections of specific groups with same volumes. \( x \) and \( y \) respectively represent the quantity of \( A \) and \( B \). The code numbers of ‘hydrophilic generation-hydrophobic generation’ are used below to concisely describe various types of models. For example, the model ‘2-3’ means the model \( A_7B_{15} \) of which the hydrophilic generation is 2 and the hydrophobic generation is 3. In addition, particles \( S \) are used in this paper to represent a collection of water molecules which is equivalent in volume to \( A \) and \( B \) particles.

Groot and Warren [12] have reported that the interaction parameters between DPD particles can be calculated from the relation between \( \alpha \) and Flory-Huggins interaction parameter \( \chi \):

\[
\alpha_y = \alpha_u + 3.27\chi_u
\]

The value of interaction parameter \( \alpha_{uu} \) between the same kind of particles is set as 25. It is difficult to measure the interaction parameter \( \chi \) between all the particles through experiments, but the all-atom molecular dynamics simulation provides a convenient way to obtain the interaction parameter \( \chi \), which is based on the calculation of cohesive energy. According to the above-mentioned particle parameters and the molecular dynamics simulation results in the references, appropriate values are selected for the DPD interaction parameters between different types of particles in the models, as shown in Table 1.
TABLE 1 DPD INTERACTION PARAMETERS

|          | A (Hydrophilic particles) | B (Hydrophobic particles) | S (Four water molecule) |
|----------|---------------------------|---------------------------|-------------------------|
| A        | 28                        | 45                        | 30                      |
| B        | 45                        | 28                        | 55                      |
| S        | 30                        | 55                        | 28                      |

The GW-VV algorithm is used in this paper to integrate the motion equation. To simplify the numerical processing, reduced units are used in the DPD simulation. The number density $\rho$ of the system is set as 3, $\sigma$=3, and the integration step $\Delta t =0.01$. The DPD simulation of the self-assembly of $A_xB_y$ molecules is carried out in a $40\times40\times40\text{Re}^3$ cubic box, which contains $1.92\times10^5$ coarse-grained particles, and the Galamost software package is used for simulation. Periodic boundary conditions are employed during the simulation, and the polymer volume fraction is 0.10.

In order to simulate non-covalent interactions, the following chemical reaction model is introduced:

$$xA + yB \rightarrow A_xB_y$$

In this model, the reaction probability parameter $P$ is introduced to control the reaction process, and the initiation site is located on the hydrophobic group. Before performing the dynamic self-assembly simulation, the two ends of the Janus polymer model are cut off. Then the models are distributed in the simulation box. When the initiation site of $B_y$ enters the reaction scope of the active end on $A_x$, the system generates a random number $S$. As long as $S$ is smaller than $P$ (which is pre-set), the reaction takes place to form a chemical bond, and a complete Janus particle is produced. After the above-mentioned process, the original initiation site loses its effect, so that one $B_y$ can only react with one $A_x$. Since the reaction rate is related to the effective collision probability between molecules, we can control the reaction rate of the system by adjusting the collision probability, thereby simulating the dynamic self-assembly process under different reaction rates.

3. RESULT AND DISCUSSION

3.1 Static self-assembly of $A_xB_y$

After performing static self-assembly simulations on various models with different hydrophilic and hydrophobic generations in the aqueous solution, different types of self-assembled structures are obtained, and the phase diagram of the generation changes and self-assembled structures is shown in Figure 1. The assembled structures in the phase diagram are distributed into four regions: Polymer models in phase A are mainly micellar structures, most of which are spherical micelles. Area A1 is further divided from phase A, in which dish-like and worm-like micelle structures exist. The corresponding structure in the phase B is the Toroidal structure. Phase C corresponds to the vesicle structure, and phase D is the multi-nuclear micelle structure.
Although precise structures cannot be acquired from the phase diagram quantitatively, but the instruction of regulation which correspond to the hydrophilic and hydrophobic generations is given, as shown in Table 2, so that experiments can be carried out more targetedly and the research efficiency can be improved.

**TABLE 2 HYDROPHILIC-HYDROPHOBIC RATIOS OF DIFFERENT SELF-ASSEMBLED STRUCTURES**

| Phase | Hydrophilic-Hydrophobic ratio | Hydrophilic generation | Structural features                        |
|-------|-------------------------------|------------------------|-------------------------------------------|
| A     | > 1.2                         | > 4.0                  | Mainly spherical micelles                 |
| A₁    | > 1.2                         | > 4.0                  | worm-like micelles and dish-like micelles |
| B     | 1.0                           | --                     | Toroidal structure with large holes (similar to ring junction) |
| C     | 0.10 ~ 0.50                   | 2.0 ~ 3.0              | Double-layer vesicles                     |
| D     | <0.1                          | --                     | Multi-nuclear micelle                     |

3.2 Dynamic self-assembly of AₐBₐ
After the static self-assembly structures of AₐBₐ are obtained, several models with specific structures are selected to perform the dynamic self-assembly simulation, which are listed in the following Table 3.

**TABLE 3 MODELS WHICH DYNAMIC SELF-ASSEMBLY SIMULATIONS ARE PERFORMED**

| Model   | Code number | Phase | Static self-assembled structure |
|---------|-------------|-------|---------------------------------|
| A₇B₃₁  | 2-4         | C     | Vesicle                         |
| A₇B₁₅  | 2-3         | C     | Vesicle                         |
| A₁₅B₃₁ | 3-4         | C     | Vesicle                         |
| A₇B₆₃  | 2-5         | D     | Multi-nuclear micelle           |
| A₁₅B₁₅ | 3-3         | B     | Toroidal                        |
| A₃₁B₆₃ | 4-5         | A     | Dish-like micelle               |
| A₆₃B₆₃ | 5-5         | A     | Worm-like micelle               |

The result of dynamic self-assembly simulation of vesicle models 2-3, 2-4 and 3-4 under different...
reaction probabilities is shown in Figure 2, and the cross-sectional views of dynamic self-assembly structures are presented in Figure 3. All the reaction time of simulations in this work is set as 100,000 DPD time steps, and the blue part in the cross-sectional views represents hydrophilic groups while the yellow part represents hydrophobic groups.

**Figure 2** Results of dynamic self-assembly of models 2-3, 2-4 and 3-4 under different reaction probabilities. Reaction time is 100,000 DPD time steps.

**Figure 3** Cross-sectional views of the dynamic self-assembled structures of model 2-3, 2-4 and 3-4 under different reaction probabilities. The reaction time is 100,000 DPD time steps. Spherical micelles are shown on the upper side, and the vesicle structures of each model obtained in the dynamic simulation are shown on the lower side.

When the reaction probability is very low (P=0.005), the system is merely a mixture of hydrophilic groups and hydrophobic groups, there are almost no interactions between them. The hydrophobic groups gather together, forming into spherical micelles. This type of micelles is different from the core-shell structure micelles, since the hydrophilic groups are sparsely distributed on the surface. When the reaction probability is increased to 0.025, vesicle structures begin to form in model 2-4 (Figure 3b) and 3-4 (Figure 3c), while vesicle structures only begin to form in model 2-3 after the reaction probability is further increased to 0.1 to form (Figure 3a). Except for spherical micelles, the structures obtained by dynamic self-assembly of these three types of models are the same as those acquired through static self-assembly, the introduction of reactions does not change their self-assembly structure.

The dynamic self-assembly structures of model 2-5, 3-3, 4-5 and 5-5 under different reaction probabilities are summarized in Figure 4. When the reaction probability is low (P=0.005), atypical spherical micelles without core-shell structures are formed in the above-mentioned models during dynamic self-assembly. When the reaction probability P>0.005, the dynamic self-assembled structures
of model 2-5 are multi-nuclear micelles (Figure 5), which are the same as those of static self-assembly, but the dynamic self-assembled nuclear structures are less obvious than those in the multi-nuclear micelles obtained by static self-assembly.

![Dynamic self-assembly structures of models 2-5, 3-3, 4-5 and 5-5 under different reaction probabilities.](image)

Figure 4 Dynamic self-assembly structures of models 2-5, 3-3, 4-5 and 5-5 under different reaction probabilities.

![Cross-sectional diagrams of the dynamic self-assembled structures of model 2-5 when the reaction probability P=0.005 and P=0.05.](image)

Figure 5 Cross-sectional diagrams of the dynamic self-assembled structures of model 2-5 when the reaction probability P=0.005 and P=0.05.

However, the dynamic self-assembled structures of the other three models have shown different results from the corresponding static self-assembled structures. As for Models 3-3 and 4-5, Toroidal structures and dish-like micelle structures are formed under static self-assembly conditions. Nevertheless, in dynamic self-assembly, vesicle structures (Figure 6) occur in the systems of these two models when the reaction probability is larger than 0.075. The dynamic self-assembled structures of models 5-5 after the reaction is introduced are all spherical micelles rather than worm-like micelles, which are obtained by static self-assembly, showing that the introduction of non-covalent interactions can regulate the self-assembly behavior of the models above.

![Cross-sectional views of the dynamic self-assembled structures of models 3-3, 4-5 and 5-5 when the reaction probability P=0.3.](image)

Figure 6 Cross-sectional views of the dynamic self-assembled structures of models 3-3, 4-5 and 5-5 when the reaction probability P=0.3.
Kinetic process of the dynamic self-assembly of model 2-3 when the reaction probability $P=0.005$ is shown in figure 7: Phase separation first occurs in the system, the hydrophobic groups gather with each other, and the reaction takes place between the hydrophilic groups and hydrophobic groups (Figure 7a); Then Toroidal metastable structures are formed in the system (Figure 7b), with sparse hydrophilic groups distributed on the surface, which are formed by the aggregation of Janus particles (generated by the reaction) and a large quantity of hydrophobic groups. With the pores gradually closed, the hydrophilic groups which are distributed on the surface of the hydrophobic aggregates are expelled (Figure 7c, Figure 7d), and the micellar structures are formed.

![Figure 7](image)

**Figure 7** Cross-sectional view of kinetic process of dynamic self-assembly of model 2-3 when the reaction probability $P=0.005$.

Kinetic process of the dynamic self-assembly of model 2-3 when the reaction probability $P$ rises to 0.2 is shown in figure 8: After the reaction probability rises, the number of Janus particles generated by the reaction increases, and more hydrophilic groups are distributed on the surface of the metastable structures, forming into a membrane structure; Then cavities with hydrophilic groups are formed during the further evolution of the metastable structures, and vesicle structures are finally formed.

![Figure 8](image)

**Figure 8** Cross-sectional view of kinetic process of dynamic self-assembly of model 2-3 when the reaction probability $P=0.005$.

The processes of vesicle formation of model 2-4 and 3-4 are similar to that of model 2-3 in this dynamic self-assembly simulation. When the reaction probability is 0.005, bowl-like structures with small openings are formed during dynamic self-assembly, then the hydrophilic groups are expelled and vesicle structures are obtained.

The results better present the dynamic self-assembly process of Janus-type amphiphilic dendrimers, which is beneficial to further understand the actual process of self-assembly and could play a certain guiding role in relevant experimental works.

4. CONCLUSION

In this research, a series of coarse-grained models $A_xB_y$ of Janus type amphiphilic dendrimers with different hydrophilic-hydrophobic generation ratios were constructed through the DPD simulation, and the static self-assembly and dynamic self-assembly simulations were performed respectively to obtain self-assembled structures with different morphologies. Two main conclusions are drawn from this study. Firstly, during static self-assembly, when the hydrophilic-hydrophobic generation ratio of Janus type amphiphilic dendrimer is within the range of 0.1–0.5, the vesicle structure can be obtained in a wide phase space; When the ratio is larger than 1, only micelles can be formed through static self-assembly of $A_xB_y$. It is easier to obtain special structures such as Toroidal in the areas close to the diagonal of the phase diagram. When the hydrophilic-hydrophobic ratio is smaller than 0.1, $A_xB_y$ mainly forms into multi-nuclear micelle structures.
Secondly, the introduction of chemical reaction model does not bring about new self-assembly structures in the models of which the static self-assembly structures are vesicles or multi-nuclear micelles, but generates new dynamic self-assembly structures for the models in the area A1 (worm-like micelles and dish-like micelles) and phase B (Toroidal structure) of the phase diagram. In the simulations during which vesicles are formed, the kinetic process can be described as follow: First, phase separation occurs and disordered aggregates are formed, then microphase separation takes place, leading to a vesicle-like metastable structure with pores on it. The pores are subsequently closed and vesicles are finally formed. In these models, the process of micelle formation during dynamic self-assembly with low reaction probability is similar to that of vesicle formation, but the hydrophilic groups are gradually expelled when the pores in the metastable structure are closed.

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REFERENCES
[1] M. Yang, W. Wang, F. Yuan, et al. Soft vesicles formed by diblock codendrimers of poly(benzyl ether) and poly(methallyl dichloride) [J]. Journal of the American Chemical Society, 2005, 127(43): 15107-15111.
[2] V. Percec, D. A. Wilson, P. Leowanawat, et al. Self-assembly of janus dendrimers into uniform dendrimersomes and other complex architectures[J]. Science, 2010, 328(5981): 1009-1014.
[3] L. Hong, A. Cacciuto, E. Luiten, Clusters of charged Janus spheres[J]. Nano Letters, 2006, 6(11): 2510-2514.
[4] D. Xu, L. Zhao, K. Zhang, et al. Dynamic self-assembly of block copolymers regulated by time-varying building block composition via reversible chemical reaction[J]. Science China (Chemistry), 2019, 62(12): 16661674.
[5] JM VA. Koelman, P. J. Hoogerbrugge, Dynamic simulations of hard-sphere suspensions under steady shear[J]. Europhysics Letters, 1993, 21(3): 363-368.
[6] P. J. Hoogerbrugge, JM VA. Koelman, Simulating microscopic hydrodynamic phenomena with dissipative particle dynamics[J]. Europhysics Letters, 1992, 19(3): 155-160.
[7] R. D. Groot, P. B. Warren, Dissipative particle dynamics: bridging the gap between atomisti and mesoscopic simulation[J]. Journal of Chemical Physics, 1997, 107(11): 4423-4435.
[8] B. Duenweg, W. Paul, Dynamics simulations without Gaussian random numbers[J]. International Journal of Modern Physics C, 1991, 2(3): 817-827.
[9] P. Espanol, P. Warren, Statistical-mechanics of dissipative particle dynamics[J]. Europhysics Letters, 1995, 30(4): 191-196.
[10] R. D. Groot, T. J. Madden, Dynamic simulation of diblock copolymer microphase separation[J]. Journal of Chemical Physical, 1998, 108(20): 8713-8724.