

Dynamics of Attractive Vesicles in Shear Flow^{*}

Zhen-yu Deng, Dong Zhang and Lin-xi Zhang^{**}

Department of Physics, Zhejiang University, Hangzhou 310027, China

Abstract A nonequilibrium molecular dynamics (NEMD) method is employed to study the dynamics of two identical vesicles with attractive interactions immersed in shear flow. The dynamics behaviors of attractive vesicles depend on the attractive interactions and the shear rates simultaneously. There are four motion types for attractive vesicles in shear flow: a coupled-tumbling (CTB) motion, a coupled-trembling (CTR) motion, a collision/rotation mixture (CRM) motion and a separated-tank-treading (STT) motion, which are determined by the competition between the shear flow and the attractive interactions. Furthermore, the dynamics behavior of an individual vesicle shows three main motion types such as tumbling, trembling and tank-treading motions, and relies mainly on the shear rates. Meanwhile, comparisons with rigid vesicles for the dynamics behaviors are made, and the collision/rotation mixture (M) motion isn't observed for rigid vesicles.

Keywords: Attractive vesicles; Shear flow; Nonequilibrium molecular dynamics.

INTRODUCTION

The dynamics of soft objects such as liquid droplets, elastic capsules, vesicles, and red blood cells in flow represents a long-standing problem in science and technology, and has received numerous attentions in theory^[1–3], simulations^[4–8] as well as experiments^[9–13]. This interest is motivated by the importance in a wide range of industries such as the pharmaceutical industry as well as in basic physiology, the most relevant of which is fundamental for understanding the complex motions of red blood cells.

The dynamics of a single vesicle is relatively well understood. These behaviors of vesicles are determined dynamically from a balance of interfacial forces with fluid stresses. Three main types of vesicle motions have been predicted theoretically and observed experimentally in presence of shear flow. These motions are characterized by intriguing shape deformations and are named tumbling (TB), trembling^[14–16] (TR) also called vacillating-breathing^[17] or swinging^[4], and tank-treading^[18, 19] (TT). The vesicle motions in shear flow depend mainly on three dimensionless parameters^[12, 20]: the capillary number measuring the flow strength over the bending energy of the membrane shape, $C_a = \eta_{out} \dot{\gamma} R^3 / \kappa = \dot{\gamma} \tau_\kappa$, the reduced volume measuring the ratio of the actual area enclosed by the vesicles over that of a sphere having the same volume, $v = [V/(4\pi/3)]/(A/4\pi)^{3/2}$, and the viscosity contrast measuring the viscosity ratio between the internal and external fluids, $\lambda = \eta_{in}/\eta_{out}$. Here τ_κ is the relaxation time scale of bending modes, $\dot{\gamma}$ is the shear rate, R is the radius of the vesicle obtained from its volume V using the sphere formula, κ is the bending modulus, A is the vesicle area, η_{in} and η_{out} are the dynamic viscosities of the internal and external fluids, respectively. The dynamics of a single vesicle is also regarded as the basis for the description of the rheology of multi-vesicle suspensions without interactions^[21, 22].

As for semi-dilute or non-dilute vesicle suspensions, the vesicle-vesicle interactions, including close-range

^{*} This work was financially supported by the National Natural Science Foundation of China (Nos. 21374102 and 21174131).

^{**} Corresponding author: Lin-xi Zhang (章林溪), E-mail: lxzhang@zju.edu.cn

Received November 18, 2015; Revised January 5, 2016; Accepted January 21, 2016

doi: 10.1007/s10118-016-1785-5

collisions and long-range dipole interactions, are proved to have significant effects on the rheology of suspensions and the orientations of vesicles. To study the dynamics of a multi-vesicle system is a challenging task for both simulations and experiments, and to date there have been few published works^[23–33]. Kantsler *et al.* have found that the binary collisions between vesicles in shear flow can cause the instantaneous inclination angle of a vesicle to deviate significantly from that in the tank-treading state, and the shear viscosity of the suspension decreases with the viscosity ratio λ when $\lambda < 1$ at 11.3% volume fraction^[23]. For comparison, the intrinsic viscosity of a vesicle suspension in the dilute limit decreases monotonically with λ in the tank-treading regime until λ approaches the critical value for the tank-treading /trembling (or tumbling) transition^[34]. Zhao *et al.* simulated multi-vesicle suspensions undergoing simple shear deformation by using the boundary-integral equation method to quantify the effects of vesicle-vesicle interactions on the microstructure and rheology of the suspension, and found that vesicle interactions in the suspension delayed the transition from tank-treading to trembling/tumbling^[34]. Gompper *et al.* employed a particle-based hydrodynamics technique to investigate the shape changes and clustering of red blood cells (RBCs) at various volume fractions under flow in cylindrical microcapillaries and reported that the RBCs had a transition from a discocyte shape at low velocities to a parachute shape at high velocities when the flow velocity increased^[32]. In their simulations, only the hydrodynamic interaction and excluded-volume repulsion between RBCs were considered, and attractive interactions between RBCs and depletion effects were excluded^[32]. Kaoui *et al.* presented numerical simulations of rheological behavior of vesicle suspensions under shear flow and proved that the viscosity of a dilute suspension of fluid-filled vesicles was a non-monotonic function of the viscosity contrast and exhibited a minimum at the critical point of the tank-treading-to-tumbling transition^[26].

Besides hydrodynamic interactions in vesicle suspensions, there exist other attractive interactions between vesicles such as long-range electrostatic and electrodynamic interactions^[35]. It is known, for example, that long-range electrodynamic interactions are strong enough to explain multilayer stacking of phospholipid bilayers^[35]. Under limited conditions, these interactions are observed between erythrocytes and substrates. Meanwhile, short-range interactions between specific chemical groups such as particular molecular receptors, antigens, bridging agents, *etc.* can create strong and specific cell contact^[36]. Furthermore, for adhesively or attractively interacting elastic vesicles, the stretching or bending of the bilayer membrane can form flat regions in the contact zone and result in an enhanced interacting energy significantly stronger than that of the rigid vesicles^[37]. Moreover, experiments have found that shear force may enhance bacterial adhesion to target cells^[38]. Motivated by these facts, we adopt a nonequilibrium molecular dynamics (NEMD) method^[39] to study the dynamics of attractively interacting vesicles suspended in shear flow, of which very few studies have been carried out previously, and our aim is to investigate the effects of attractive interactions on the dynamics behaviors of multi-vesicles in shear flow.

MODEL AND METHODS

Vesicle Model

We model the elastic vesicle by employing the fishnet-like network, in which the bead positions on the vesicle surface are acquired by a triangular network^[40]. To prevent overlap between any two beads on the same vesicle surface, the beads interact with each other *via* a purely repulsive truncated and shifted Lennard-Jones potential

$$U_{\text{LJ}} = \begin{cases} 4\varepsilon[(\frac{\sigma}{r})^{12} - (\frac{\sigma}{r})^6 + \frac{1}{4}] & r \leq r_c \\ 0 & r > r_c \end{cases} \quad (1)$$

where r is the distance between the centers of two beads on the same vesicle surface, σ is the bead diameter, the cutoff distance r_c is set to $2^{1/6}\sigma$ and $\varepsilon = 1.0 k_B T$.

The neighboring beads on the vesicle surface are connected with the harmonic potential

$$U_{\text{bond}} = \frac{k_b}{2} (r - r_0)^2 \quad (2)$$

where $r_0 = 1.0\sigma$ is the equilibrium bond distance, and $k_b = 160 k_B T / \sigma^2$ is a spring constant.

The bending rigidity of the vesicle surface is modeled by a dihedral potential between adjacent triangles^[41, 42]

$$U_{\text{bending}} = K_b (1 + \cos \phi) \quad (3)$$

where ϕ is the dihedral angle between opposite vertices of any two triangles sharing an edge, and K_b is the bending energy constant.

The attractive interactions between two beads on two different vesicle surfaces are given by the shifted and truncated 6-12 Lennard-Jones (LJ) potential

$$U_{\text{LJ}}^{\text{attractive}} = \begin{cases} 4D_0 \left[\left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^6 + \frac{1}{4} \right] & r \leq r'_c \\ 0 & r > r'_c \end{cases} \quad (4)$$

where D_0 is the binding energy, and $r = |\mathbf{r}_i - \mathbf{r}_j|$ denotes the spatial distance between beads i and j located at $\mathbf{r}_i$ on one vesicle surface and $\mathbf{r}_j$ on another vesicle surface, respectively. The cutoff distance r'_c is chosen to be 1.5σ in order to ensure that their interactions are attractive. Two identical vesicles are initially located randomly in a fluid of LJ particles with the same diameter of σ at a density of $\rho\sigma^3 = 0.85$. Here the excluded volume effect is considered by adopting the purely repulsive truncated and shifted Lennard-Jones potential, *i.e.*, Eq. (1), for fluids of LJ particles. Both the two vesicles are filled with inner fluid particles at the same density of the outer fluid. All the inner fluid particles are kept inside the vesicle membrane, and both outer and inner fluid particles are not allowed to penetrate through the membrane during the process of dynamics. To achieve the shear flow condition, we enforce the velocity boundary conditions^[43]. The upper wall moves with a velocity of $-V_x$ and the bottom wall with a velocity of V_x . The shear rate can be derived from $\dot{\gamma} = 2V_x/\Delta z$, where Δz is the channel width. Although there are some previous works taking shear rate as a controlling parameter to study dynamics of vesicles or polymers in shear flow^[11, 19], the Reynolds number has another definition as the reduced shear rate which is the multiplication of relaxation time and shear rate to make the parameter dimensionless^[44], *i.e.*, $\text{Re} = \rho R_0^2 \dot{\gamma} / \eta_0$. The density of both internal and external fluids is 0.85, with a vesicle radius of $R_0 = 6.21\sigma$. The viscosity of solvent fluids can be derived from $\eta_0 = 20.1(mk_B T)^{1/2}/a^2$ for the vesicle of $K_b = 20k_B T$ ^[45, 46]. Therefore, the Reynold number can be expressed in the form of $\text{Re} = 1.63 \dot{\gamma}$, and the maximum value of Reynold number is about 0.82 for a maximum shear rate of $\dot{\gamma} = 0.6/\tau_0$ in our simulation. The box size is set to $40\sigma \times 40\sigma \times 40\sigma$ (*i.e.*, 3D dimensional model), and periodic boundary conditions are applied in the x and y directions. In fact, there are two walls in the z direction in our model, and it is important to choose a suitable distance of two walls. If a short distance of two walls is chosen, the effects of the walls can't be ignored, and if a long distance is chosen, two vesicles are far away from each other, and there doesn't exist attractive interactions between vesicles because it is short-range interaction. Therefore, a distance of 40σ is chosen. As our aim here is to investigate the effects of attractive interactions on the dynamics behavior of vesicles, other effects such as the distance of walls aren't considered.

NEMD Method

In our NEMD method, the DPD (dissipative particle dynamics) thermostat is used to maintain the temperature of the fluid at a desired value. The equations of motions are given by^[39, 47-49].

$$\ddot{\vec{r}}_i = \frac{\vec{F}_i}{m_i} \quad (5)$$

$$\vec{F}_i = \vec{F}_i^C + \vec{F}_i^D + \vec{F}_i^R \quad (6)$$

where $\vec{F}_i^C$ is a conservative force, which is calculated from LJ, harmonic, binding and bending potentials, $\vec{F}_i^D$ is a dissipative force, and $\vec{F}_i^R$ is a random force. The dissipative and the random forces are defined as follows:

$$\vec{F}_{ij}^D = -\zeta w^D(r_{ij})(\hat{r}_{ij} \cdot \vec{v}_{ij})\hat{r}_{ij} \quad (7)$$

$$\vec{F}_{ij}^R = \mu w^R(r_{ij})\theta_{ij}\hat{r}_{ij} \quad (8)$$

where $\hat{r}_{ij}$ is the unit vector in the direction $\vec{r}_{ij} = \vec{r}_i - \vec{r}_j$ with $r_{ij} = |\vec{r}_{ij}|$, and $\vec{v}_{ij} = \vec{v}_i - \vec{v}_j$ is the relative velocity vector of the two beads i and j . μ is a coefficient characterizing the noise strength of the random forces, and ζ is a coefficient which controls the extent of dissipation in a simulation time step. w^D and w^R are r -dependent weight functions that describe the range of dissipative and random forces and vanish for $r > r_c$. θ_{ij} is a Gaussian variable with zero mean and variance equal to τ^{-1} , where τ is the time step. Either of the two weight functions in Eqs. (9) and (10) can be chosen arbitrarily, while the other must satisfy the following relations:

$$w^D(r) = [w^R(r)]^2 \quad (9)$$

$$\mu^2 = 2k_B T \zeta \quad (10)$$

We set $\zeta = 1$ for both the inner and the outer flows. For simplicity, the weight functions in this simulation are

$$w^D(r) = [w^R(r)]^2 = \begin{cases} (1 - r/r_c)^2 & r \leq r_c \\ 0 & r > r_c \end{cases} \quad (11)$$

The none-equilibrium molecular dynamics (NEMD) has also been adopted in many simulations. Our simulation method originates from DPD method and replaces the conservative force with LJ repulsive force between fluid particles to avoid density fluctuation near wall boundary^[39]. Their DPD simulation results showed that DPD thermostat can simulate dynamics behaviors of fluids under shear flows^[39]. The simulations are performed using the open source LAMMPS molecular dynamics package^[50] in the NVT ensemble. The NVT ensemble is widely adopted in molecular dynamics simulation as well as statistical physics, in which the number of particles (N), the volume (V) and the temperature (T) of the system are constant. The temperature is set to $T = 1.0$, and the time step is $\tau = 0.0001\tau_0$, where $\tau_0 = (m\sigma^2/k_B T)^{1/2}$ is the time unit in our simulation. Each simulation runs at least 3×10^7 steps. As The standard reduced LJ units, in terms of which all physical quantities are expressed, are used in the simulation, namely, m , σ , ε , $T = \varepsilon/k_B$, as the mass, length, energy, and temperature scales, respectively. All statistical properties are averaged over 20 runs, and similar results can be obtained for each run with different initial location of the two identical vesicles. Meanwhile, the number of beads on vesicle surface is 642 for the radius of vesicle $R = 6.21\sigma$ ^[40], and the radius of vesicle is the same as the effective radius of vesicle of $R = 5.7\sigma$ in the simulation of RBCs under flow in cylindrical microcapillaries^[32]. Similar simulation results are obtained for a choice of large vesicle size.

RESULTS AND DISCUSSION

Dynamics of Attractive Elastic Vesicles

We first study dynamics of two attractive elastic vesicles with $K_b = 20$ under shear flow. Dynamics behaviors of attractive vesicles depend on the binding energy D_0 and the shear rate $\dot{\gamma}$ simultaneously, as shown in Fig. 1, and Fig. 2 gives snapshots at different simulation times for attractive vesicles with various motion types. The snapshots of the two vesicles at different simulation times in Fig. 2 are shown after the system runs about 1.5×10^7 steps, and similar snapshots of the two vesicles are observed for each run with different initial location of the two identical vesicles. Therefore, the snapshots of two vesicles at different simulation times are independent of the initial location of the two identical vesicles. For a given binding energy D_0 , at a relatively low

flow, the two vesicles are closely adhered to each other and well synchronized, and the aggregated vesicles exhibit an anticlockwise tumbling motion that arises from the flow velocity gradient, defined as the coupled-tumbling (CTB) motion, see Figs. 1 and 2. At a high shear rate, see Fig. 1, two vesicles perform a separated-tank-treading (STT) motion. Each vesicle deforms into an ellipsoidal shape at a stationary orientation along the

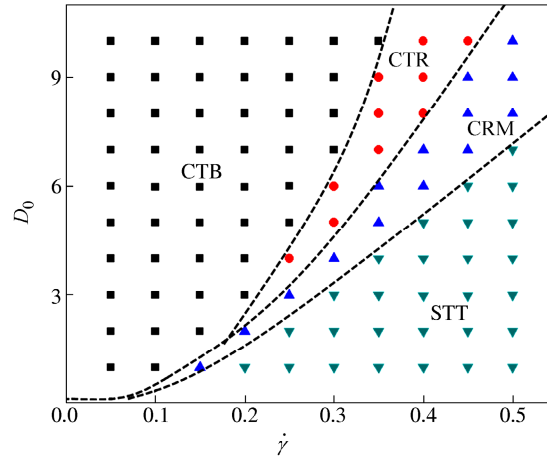


Fig. 1 A phase diagram showing dynamics behaviors of two attractive elastic vesicles in shear flow with respect to the shear rate $\dot{\gamma}$ and the binding energy D_0 between two vesicles

The symbols depict four motion modes: the coupled-tumbling (CTB, squares), coupled-trembling (CTR, circles), collision/rotation mixture (CRM, uptriangles) and separated-tank-treading (STT, cyan downtriangles).

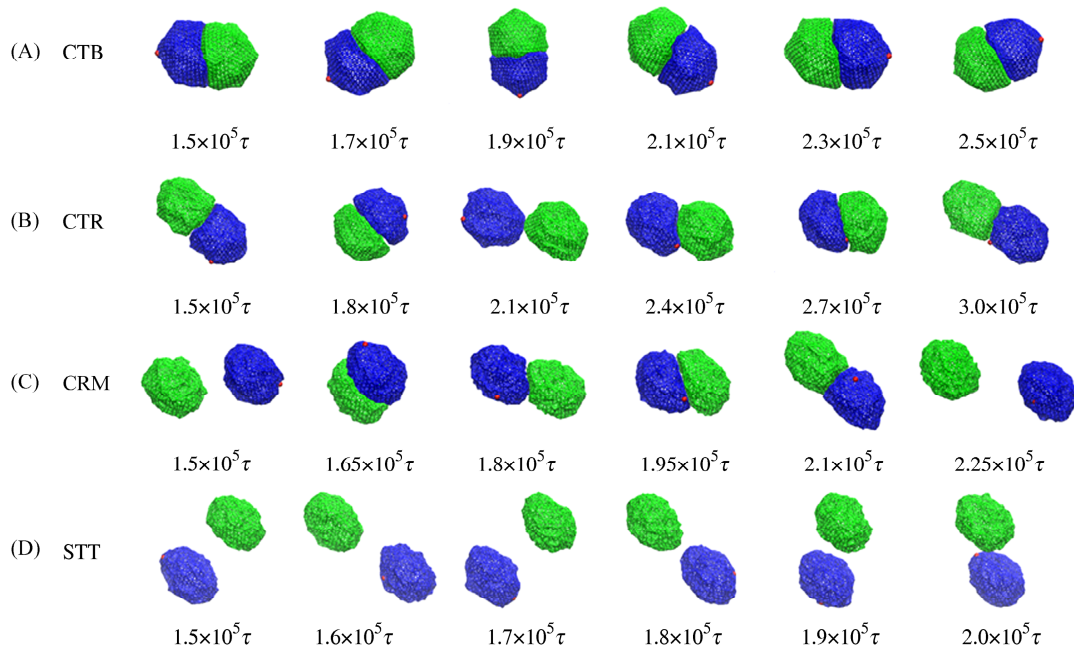


Fig. 2 Snapshots at different simulation times for two attractive vesicles with various shear rates and binding energies: (A) a coupled-tumbling (CTB) motion with $\dot{\gamma} = 0.1$ and $D_0 = 5$, (B) a coupled-trembling (CTR) motion with $\dot{\gamma} = 0.3$ and $D_0 = 5$, (C) a collision/rotation mixture (CRM) motion with $\dot{\gamma} = 0.5$ and $D_0 = 10$ and (D) a separated-tank-treading (STT) motion with $\dot{\gamma} = 0.5$ and $D_0 = 3$

flow direction with its membrane circulating about the vesicle interior. Two separated vesicles migrate at a nearly symmetric trajectory with transient and frequent collisions, see Fig. 2. In the moderate shear rates regions, the coupled-trembling (CTR) and the collision/rotation mixture (CRM) motions are observed, see Figs. 1 and 2. In the coupled-trembling (CTR) motion, the overall aggregated vesicles undergoes a periodic unsteady flipping motion known as tumbling, whereas each composed vesicle trembles with large shape fluctuations and angular oscillation around a fixed inclination. The shear rate induces relative slide along the vesicle contact area, however, two vesicles aren't separated completely, see Fig. 2. With the shear rate further increases, the collision/rotation mixture (CRM) motion is observed. The two vesicles are aggregated due to the attractive interactions and rotate around each other, and then are separated at a preferred orientation, see Fig. 2.

To analyze the dynamics process of two attractive vesicles in detail, we first present some statistical properties on the CTB motion and focus on different dynamics behaviors between the aggregated vesicles and the composed vesicle. Figure 3(a) shows time evolution of the total adsorption energy U , the contour shape factor δ and the contour inclination angle θ of the aggregated vesicles, as well as the shape factor δ' and the inclination angle θ' of an individual vesicle for CTB motion with $\dot{\gamma} = 0.1$ and $D_0 = 5$. The shape factor δ is the degree of deviation from a spherical shape^[44–54],

$$\delta = \frac{(\lambda_1 - \lambda_2)^2 + (\lambda_2 - \lambda_3)^2 + (\lambda_1 - \lambda_3)^2}{2R_g^4} \quad (12)$$

where $\lambda_1 \leq \lambda_2 \leq \lambda_3$ are the eigenvalues of the moment-of-inertia tensor (with corresponding eigenvectors $\mathbf{u}_1$, $\mathbf{u}_2$, and $\mathbf{u}_3$) and the squared radius of gyration $R_g^2 = \lambda_1 + \lambda_2 + \lambda_3$. This is a convenient measure to distinguish various shapes, where $\delta = 0$ for sphere, 1 for thin rods, and 0.25 for thin disks^[51]. Meanwhile, the inclination angle θ is given by $\theta = \arctan(u_3^x/u_3^z)$ where $\mathbf{u}_3 = (u_3^x, u_3^y, u_3^z)$ is the eigenvector of the moments-of-inertia tensor with the largest eigenvalue. When we calculate the shape factor δ' and the inclination angle θ' of an individual vesicle, a vesicle is chosen randomly because there are two vesicles in our system. In Figs. 3(A-I) and 3(A-II), it can be distinctly seen that both θ and θ' increase monotonically with time from 0 to π in a constant period T , indicating that both the aggregated vesicles and the individual vesicle undergo a tumbling motion. As shown in Figs. 3(A-III) and 3(A-IV), δ is negatively associated with δ' . When δ reaches its local maximum value ($\delta = \delta_{\max}$), δ' becomes the minimum one ($\delta' = \delta'_{\min}$), and the two vesicles share the largest contact area, which can result in the maximum adsorption energy $U = U_{\max}$. Similarly, the valleys in the δ - t curve correspond to the peaks in the δ' - t curve, where the total adsorption energy U becomes the lowest. The contour shape factor of the aggregated vesicles increases gradually from $\delta = 0.04$ to 0.07, while the shape factor of an individual vesicle decreases from $\delta' = 0.03$ to 0.01. Figure 3(b) gives a brief schematic illustration to explain this phenomenon. When θ increases monotonically due to the effects of shear flow for $\theta < \pi/2$, the shear flow contributes to the adhesion of two vesicles, the two vesicles are likely to be squeezed by the shear flow into a more spherical shape, and these two vesicles undergo large deformations with sharing the larger flattening contact area, see Fig. 3(B-a). And there exists a critical contour inclination angle θ_{c2} for the aggregated vesicles (with respect to a critical inclination θ'_{c2} for the individual vesicle) with $\delta = \delta_{\min}$. When $\theta > \pi/2$, the shear flow tends to separate these two vesicles while the attractive interactions between two vesicles can partially compensate the separation of two vesicles. Therefore, the whole aggregated vesicles are elongated by the shear flow with $\delta = \delta_{\max}$ whereas the individual vesicle becomes spherical with $\delta' = \delta'_{\min}$, see Fig. 3(B-b). In contrast, there also exists a critical contour inclination angle θ_{c1} for the aggregated vesicles (with respect to θ'_{c1} for an individual vesicle) with the maximum deformation. Figure 3(c) shows the average tumbling period $\langle T \rangle$ as a function of shear rate $\dot{\gamma}$, and it is a weak power-law dependence of $\dot{\gamma}$ with an exponent of -0.77 . This trend is consistent with the Keller-Skalak theory^[55]: $\langle T \rangle = 2\pi(\alpha + \alpha^{-1})/\dot{\gamma}$, where α denotes the aspect ratio. Moreover, the critical inclination angles θ_{c1} , θ'_{c1} , θ_{c2} and θ'_{c2} also depend on the shear rate $\dot{\gamma}$. Figure 4(a) shows that θ_{c1} increases from $\theta_{c1} = 2.28$ to 2.56 when the shear rate $\dot{\gamma}$ increases from $\dot{\gamma} = 0.05$ to 0.25, accompanied by a large shape deformation for the whole aggregated vesicles, whereas θ_{c2} slightly decreases with the whole

aggregated vesicles exhibiting a more spherical shape due to the “pinching” of the shear flow. Figure 4(b) gives that θ'_{c2} fluctuates as the shear rate $\dot{\gamma}$ increases, and a sharp increase occurs for θ'_{c1} in the region of $\dot{\gamma} = 0.1$ – 0.15 because the main axis of the individual vesicle changes for the shear rates increasing from 0.1 to 0.15, see the inset in Fig. 4(b). The schematic illustrations about these dependences of the critical inclination angles on the shear rate are shown in Figs. 4(a) and 4(b).

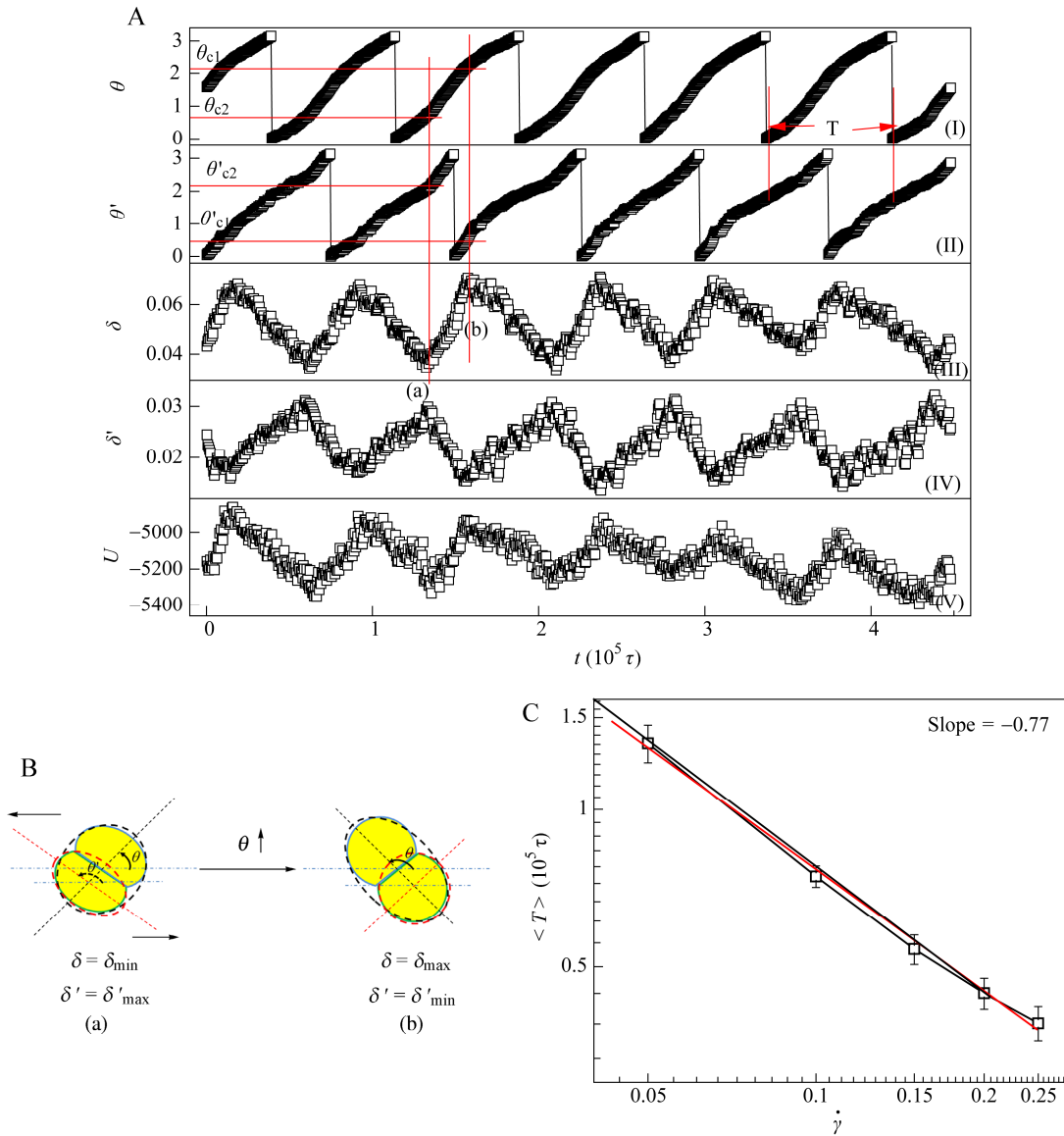


Fig. 3 (A) Time evolution of the contour inclination angle θ and the contour shape factor δ of the aggregated vesicles as well as the inclination angle θ' and the shape factor δ' of individual vesicle, and the total adsorption energy U in a coupled-tumbling (CTB) motion with $\dot{\gamma} = 0.1$ and $D_0 = 5$ (For a given shear rate and binding energy, there exist critical values of θ and θ' at the peak and the valley in the δ - t curve, labeled as θ_{c1} , θ'_{c1} , θ_{c2} , θ'_{c2}); (B) A schematic illustration showing that the contour of aggregated vesicles becomes more aspherical with the increase of θ from (A) to (B); (C) The average tumbling period $\langle T \rangle$ as a function of the shear rate $\dot{\gamma}$ at a binding energy of $D_0 = 5$

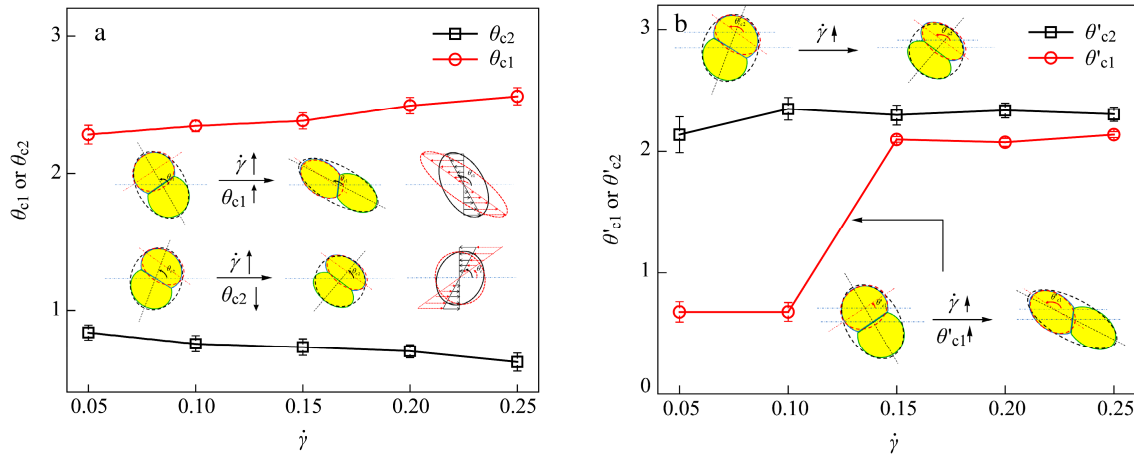


Fig. 4 The critical contour inclination angles of the aggregated vesicles θ_{c1} and θ_{c2} (a) and the individual vesicles θ'_{c1} and θ'_{c2} (b) as a function of the shear rate $\dot{\gamma}$ at a binding energy of $D_0 = 5$

With the increase of shear rate, the two vesicles are no longer tightly adhered to each other and their motions become asynchronous. As the shear rate isn't large enough to overcome the attractive interactions, the two vesicles can't be separated and present a CTR motion, which is typically shown in Fig. 5 with $\dot{\gamma} = 0.3$, and $D_0 = 5$. The aggregated vesicles substantially exhibit a tumbling motion, and can maintain a stationary orientation for a long time during a tumbling period, which corresponds to the plateaus in the θ - t curve, see Fig. 5(A-I). However, the individual vesicle undergoes a noticeable angular oscillation from 2.05 to 2.75, with the vesicle surface circulating about the interior. Similar to the CTB motion, when the contour shape factor δ reaches the minimum value, the shape factor of an individual vesicle δ' is maximum and the total adsorption energy U is minimum. Note that the minimum value of δ is about 0.025, which is smaller than that in the CTB motion shown in Fig. 3(A). Whereas the maximum value of δ is about 0.36, which is much larger than that in the CTB motion with $\dot{\gamma} = 0.1$, and $D_0 = 5$, this means that the shape of the aggregated vesicles has been elongated greatly. Therefore, the larger the shear rate is, the more fluctuation the shape of the aggregated vesicles is. Meanwhile, the maximum value of total adsorption energy U is about $U_{\max} = -400k_B T$, demonstrating that the two vesicles are not separated and still share a small contact area because $U_{\max}$ isn't close to 0. A schematic illustration of the CTR motion is shown in Fig. 5(B). The elongating and "pinching" effects of the shear flow are similar to those in the CTB motion, however, during the "pinching" period, a stringent translating motion of the aggregated vesicles is observed while the surface of an individual vesicle tank-treads. During the translating period, due to the temporary balance between the shear flow and the adsorption energy, the contour shape factor δ and the contour inclination angle θ are almost constant, see Figs. 5(B-b) and 5(B-c), while the vesicle surface and the internal fluid of the individual vesicle circulate. Both the shear flow and the attractive interactions induce the two vesicles to approach, with θ keeping the constant and δ decreasing, see Figs. 5(B-c) and 5(B-d). Finally, when the two vesicles are close enough, the aggregated vesicles continue to rotate anticlockwise, and migrate in the flow, see Figs. 5(B-d) and 5(B-a).

As the shear rate further increases, the shear flow prevails and can induce the two vesicles to be separated. The separated vesicles collide again as a result of the periodic boundary condition and the two vesicles may rotate around each other for integer times of half turn, then the two vesicles are separated again, exhibiting a collision/rotation mixture (CRM) motion. When the shear rate becomes sufficiently large, the shear flow dominates, and the two vesicles undergo a tank-treading motion separately and collide transiently but frequently in the transverse direction due to periodic boundary conditions, which is defined as a separated-tank-treading (STT) motion. Figure 6(a) shows the time dependence of some parameters that characterize the two motion types of CRM and STT: the minimum distance between two vesicles d_m ; the total adsorption energy U ; the

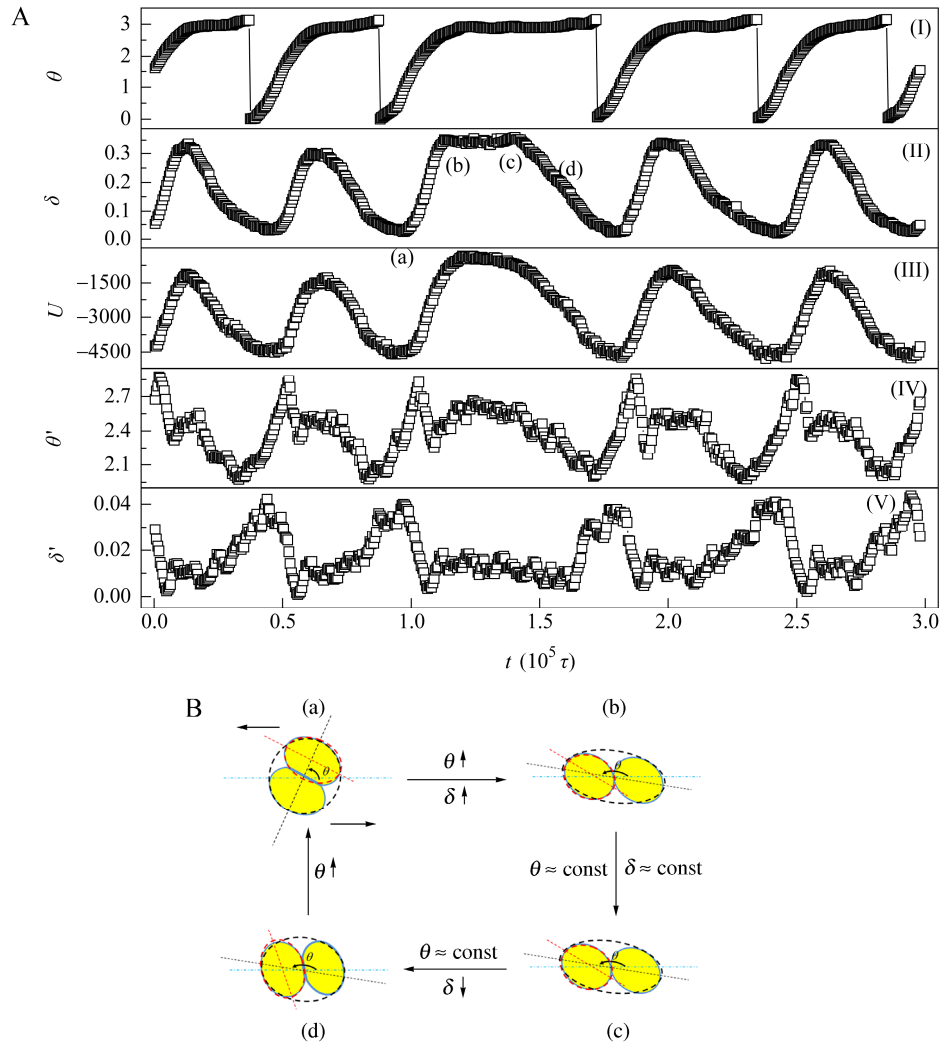


Fig. 5 (A) Time evolution of the contour inclination angle θ and the contour shape factor δ of the aggregated vesicles as well as the inclination angle θ' and the shape factor δ' of individual vesicle, and the adsorption energy U in a coupled-trembling (CTR) motion with $\dot{\gamma} = 0.3$ and $D_0 = 5$; (B) A schematic illustration showing a complex dynamical behavior of two attractive vesicles during a period of the coupled-trembling (CTR) motion

distance d_i of an individual vesicle to the initial midpoint of the two vesicle centers in the z -direction; the inclination angle of an individual vesicle θ' . The left column shows the results for the CRM motion with $\dot{\gamma} = 0.35$ and $D_0 = 5$, and the right one gives the results for the STT motion with $\dot{\gamma} = 0.5$ and $D_0 = 5$. From Fig. 6(a), it can be clearly seen that there are two modes in the CRM motion: collision mode and rotation mode. In the typical rotation process of two vesicles, d_m keeps a constant of 1.0, which corresponds to the minimum distance of two beads with considering excluded volume effect in our simulation, whereas the total adsorption energy U oscillates but cannot reduce to be 0 indicating that the two vesicles are adhered. The values of d_i for the two vesicles intersect during the rotation process, namely, the two aggregated vesicles rotate around each other for a full turn and a half turn in the regions (I) and (II), respectively. This time-dependence obtained in simulations is in agreement with experimental results^[23]. In fact, the hydrodynamic interaction of two identical capsules enclosed by thin shells with oblate spheroidal and biconcave unstressed shapes in simple shear flow can also induce capsules to rotate around each other^[8]. In the simple collision process, d_m , U and d_i oscillate periodically.

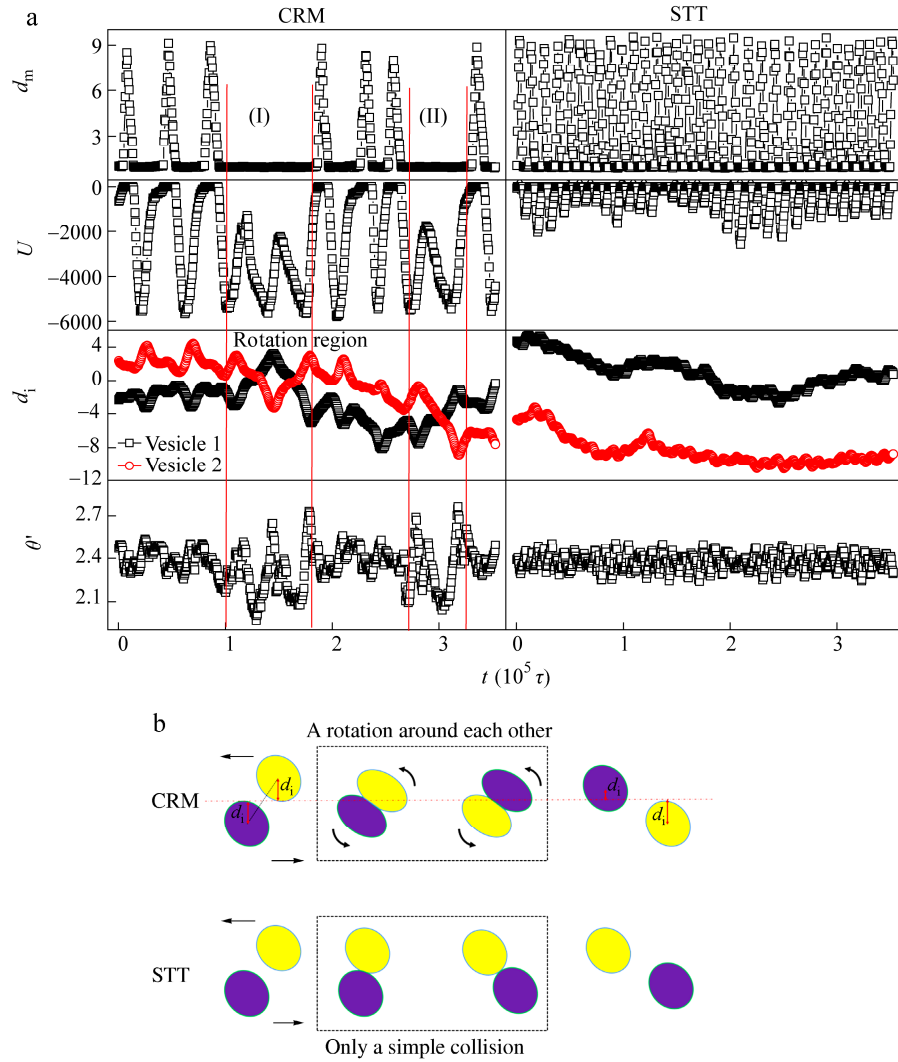


Fig. 6 (a) Time evolution of the minimum distance between two different vesicles d_m , the total adsorption energy U , the distance of the center of an individual vesicle to the midpoint of the two vesicle centers in the z -direction d_i , and the shape factor θ' of individual vesicle in the collision/rotation mixture (CRM) motion with $\dot{\gamma} = 0.35$, $D_0 = 5$ (left column) and in the separated tank-treading (STT) motion with $\dot{\gamma} = 0.5$, $D_0 = 5$ (right column); (b) A schematic illustration showing different motion types for attractive vesicles in the CRM and the STT motions

The total adsorption energy U decreases to zero with the minimum distance of two vesicles $d_m > 7$ and the values of d_i for the two vesicles are disjointed. Meantime, the inclination angle θ' of the individual vesicle in the rotation motion region oscillates more drastically than that in the collision motion region (Fig. 6a). However, there only consists of a simple collision in the STT motion, in which d_m oscillates periodically and U varies from -2000 to 0. The fact that the minimum adsorption U in the STT motion is much greater than that in the CRM motion means that the collision occurs very quickly and the number of contact beads between two vesicles is very small in the STT motion. Meanwhile, the value of d_i slightly oscillates owing to the collision and the fluctuation amplitude of d_i in the STT motion is much smaller than that in the CRM motion. The inclination angle θ' of an individual vesicle is almost a constant, showing that the vesicles undergo tank-treading motion individually.

In order to understand the CRM and STT motions clearly, a schematic illustration about the difference between CRM and STT motions is shown in Fig. 6(b). In the CRM motion, two vesicles may rotate around each other, which relies on the competition between the shear flow and the attractive interactions between two vesicles. The shear flow induces two vesicles to be separated whereas the attractive interactions prefer two vesicles to be aggregated. Once these two elements are in equilibrium, the rotation motion can occur, see Fig. 6(b). If the shear rate is too large, the ability to be separated is in a dominant position, a STT motion occurs, also see Fig. 6(b). Of course, if the attractive interactions are strong enough, it is very difficult for two vesicles to be separated, therefore, two motion types such as CTB and CTR can be observed.

Dynamics of Attractive Rigid Vesicles

Motivated by the fact that rigid vesicles can hardly deform by stretching or bending like elastic vesicles, we further investigate the dynamics behaviors of attractive rigid vesicles with $K_b = 5 \times 10^5$. They have been found in recent research studies, and their attractive behaviors are entirely different from those of elastic vesicles^[56]. Therefore, it is also important to study the dynamics behavior of rigid vesicles. In fact, the feature of elastic vesicles can be described by the Foppl-Von Karman number $\gamma = YR^2/K_b$, where Y is the Young's modulus of the surface, R is the radius of the vesicle, and K_b is the bending rigidity^[57]. Considering the Young's modulus of the surface Y and the radius R of vesicles are constant, we simplify the Foppl-Von Karman number $\gamma \propto K_b^{-1}$. Therefore, the vesicle with $K_b = 5 \times 10^5$ can be regarded as a rigid vesicle. The phase diagram for rigid vesicles is shown in Fig. 7. The motion types of rigid vesicles also depend on the shear rate ($\dot{\gamma}$) and the binding energy (D_0). Although two rigid vesicles can be aggregated together and exhibit a coupled-tumbling (CTB) motion at a low shear flow and two rigid vesicles undergo a separately-tumbling (STB) motion at a high shear flow, a collision/rotation mixture (CRM) motion isn't observed (Fig. 7). The CTB motion of rigid vesicles consists of two modes, one is defined as CTB(I), in which the two vesicles are well synchronized, and another is CTB(II), in which the vesicles are adhered to each other but irregular relative slides coexist. These two motion types are different from the CTB and CTR motions for elastic vesicles, as the shape factor of the aggregated rigid vesicles remains constant, and the contour inclination angle varies monotonously during a CTB process, see the results in Fig. 8.

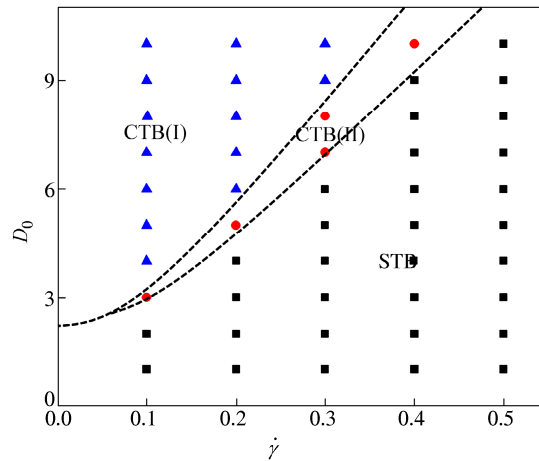


Fig. 7 A phase diagram showing dynamics behaviors of two attractive rigid vesicles in shear flow with respect to the shear rate $\dot{\gamma}$ and the binding energy D_0

The symbols depict three motion types: a coupled-tumbling without relative motion (CTB(I), uptriangles), a coupled-tumbling with relative motion (CTB(II), circles) and a separated-tumbling (STB, squares) motion

Compared with the phase diagram of attractive soft vesicles in Fig. 1, the absence of CRM motion in the phase diagram of attractive rigid vesicles is of paramount importance. The deformative property of soft vesicles

plays a dominant role in their dynamics behaviors such as rotation motion in shear flow. Previous studies about the dynamics of capsules with spherical, obstacle spheroidal, and biconcave unstressed shape in a simple shear flow showed that two spherical capsules in shear flow either cross over each other or undergo spiraling motion, however, oblate spheroidal or biconcave capsules exhibit two additional motions, namely the swapping and continuous rotation motions, which occur only when each capsule undergoes tumbling motion^[8]. Our results show that the relatively strong attractive interactions can also lead to two spherical vesicles rotating around each other. It is found that adhesive interacting elastic vesicles can form flat regions in their contact zone which enhances their attractive interactions^[37]. Both the attractive interactions and shear flow can bring about moment of force and lead to two deformative vesicles rotating around each other. Figure 9 shows time dependence of the total adsorption energy for elastic vesicles in the CRM motion with $\dot{\gamma} = 0.5$ and $D_0 = 10$, and rigid vesicles in the CTB(I) motion with $\dot{\gamma} = 0.3$ and $D_0 = 10$ as well as in the STB motion with $\dot{\gamma} = 0.5$ and $D_0 = 10$. The total adsorption energy U for elastic vesicles oscillates dramatically and has an average value of $6000k_B T$ due to a large contact area between two vesicles, and these fluctuations in contact area can induce two attractive vesicles to rotate around each other as well as bring about two attractive vesicles to be separated in the CRM motion. However, for the rigid vesicles, the total attractive interactions always keep a constant because there isn't any deformation for the rigid vesicles during the motion. This is the main reason why the motion type is relatively simpler for the rigid vesicles in shear flow.

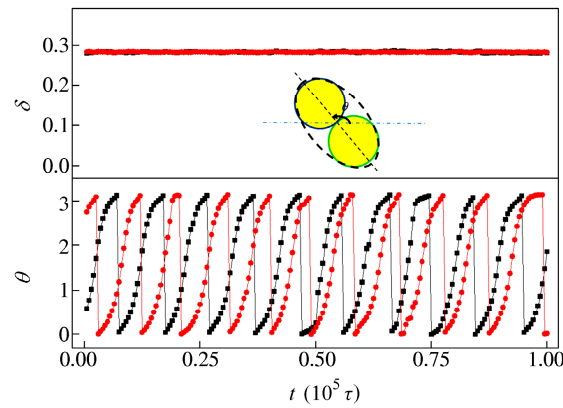


Fig. 8 Time evolution of the contour shape factor δ and the contour inclination angle θ of the aggregated rigid vesicles in the CTB(I) motion with $\dot{\gamma} = 0.1$, $D_0 = 5$ (squares) and the CTB(II) motion with $\dot{\gamma} = 0.3$, $D_0 = 5$ (circles)

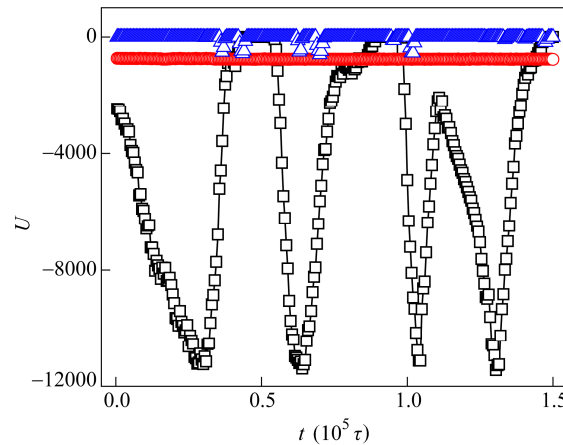


Fig. 9 Time evolution of the total adsorption energy U for elastic vesicles with $\dot{\gamma} = 0.5$, $D_0 = 10$ (squares), and for rigid vesicles with $\dot{\gamma} = 0.3$, $D_0 = 10$ (circles) and $\dot{\gamma} = 0.5$, $D_0 = 10$ (triangles), respectively

CONCLUSIONS

In this paper, we investigate the dynamics behavior of two attractive vesicles in shear flow using a nonequilibrium molecular dynamics (NEMD) method. The dynamics of interacting vesicles is governed by the competition between the shear flow and the attractive interactions. The shear flow induces the two vesicles to be separated and the attractive interactions prefer the two vesicles to be aggregated. There are four motion types for attractive vesicles in shear flow: a coupled-tumbling (CTB) motion, a coupled-trembling (CTR) motion, a collision/rotation mixture (CRM) motion and a separated-tank-treading (STT) motion. If the shear rate is high enough, the ability to be separated is in a dominant position, an STT motion occurs. Of course, if the attractive interactions are large enough, it is very difficult for the two vesicles to be separated, therefore, two motion types such as CTB and CTR can be observed. Once these two elements are in equilibrium, the rotation motion can occur. Of course, the dynamics behavior of an individual vesicle shows three main motion types such as tumbling, trembling and tank-treading motions, and relies mainly on the shear rates. As rigid vesicles can hardly deform by stretching or bending like elastic vesicles, comparisons with rigid vesicles for the dynamics behaviors are made, and the collision/rotation mixture (CRM) motion isn't observed for rigid vesicles.

REFERENCES

- 1 Barthes-Biesel, D. and Rallison, J., *J. Fluid Mech.*, 1981, 113: 251
- 2 Skotheim, J.M. and Secomb, T.W., *Phys. Rev. Lett.*, 2007, 98: 078301
- 3 Noguchi, H., *Phys. Rev. E*, 2009, 80: 021902
- 4 Noguchi, H. and Gommper, G., *Phys. Rev. Lett.*, 2007, 98: 128013
- 5 Sui, Y., Chew, Y.T., Roy, P., Chen, X.B. and Low, H.T., *Phys. Rev. E*, 2007, 75: 066301
- 6 Dodd, S.K. and Bagchi, P., *Phys. Rev. E*, 2009, 79: 046318
- 7 Bagchi, P. and Kalluri, R.M., *Phys. Rev. E*, 2009, 80: 016307
- 8 Le, D.V. and Chaim, K.H., *Phys. Rev. E*, 2011, 84: 056322
- 9 Chang, K. and Olbricht, W., *J. Fluid Mech.*, 1993, 250: 609
- 10 Fischer, T.M., *Biophys. J.*, 2004, 86: 3304
- 11 Abkarian, M., Faivre, M. and Viallat, A., *Phys. Rev. Lett.*, 2007, 98: 188302
- 12 Abreu, D., Levant, M., Steinberg, V. and Seifert, U., *Adv. Colloid Interface Sci.*, 2014, 208: 129
- 13 Deschamps, J., Kantsler, V., Segre, E. and Steinberg, V., *Proc. Natl. Acad. Sci. U.S.A.*, 2009, 106: 11444
- 14 Kantsler, V. and Steinberg, V., *Phys. Rev. Lett.*, 2006, 96: 036001
- 15 Lebedev, V., Turitsyn, K. and Vergeles, S., *Phys. Rev. Lett.*, 2007, 99: 218101
- 16 Yazdani, A.Z.K. and Bagchi, P., *Phys. Rev. E*, 2011, 84: 026314
- 17 Misbah, C., *Phys. Rev. Lett.*, 2006, 96: 028104
- 18 De Haas, K., Blom, C., Van den Ende, D., Duits, M. and Mellema, J., *Phys. Rev. E*, 1997, 56: 7132
- 19 Kantsler, V. and Steinberg, V., *Phys. Rev. Lett.*, 2005, 95: 258101
- 20 Tahiri, N., Biben, T., Ez-Zahraoui, H., Benyoussef, A. and Misbah, C., *Microvascular Res.*, 2013, 85: 40
- 21 Vlahovska, P.M. and Gracia, R.S., *Phys. Rev. E*, 2007, 75: 016313
- 22 Danker, G. and Misbah, C., *Phys. Rev. Lett.*, 2007, 98: 088104
- 23 Kantsler, V., Segre, E. and Steinberg, V., *Europhys. Lett.*, 2008, 82: 58005
- 24 Lac, E., Morel, A. and Barthès-Biesel, D., *J. Fluid Mech.*, 2007, 573: 149
- 25 Farutin, A. and Misbah, C., *Phys. Rev. Lett.*, 2013, 110: 108104
- 26 Kaoui, B., Jonk, R.J. and Harting, J., *Soft Matter*, 2014, 10: 4735
- 27 Katanov, D., Gompper, G. and Fedosov, D.A., *Microvasc. Res.*, 2015, 99: 57
- 28 Narsimhan, V., Zhao, H. and Shaqfeh, E.S.G., *Phys. Fluids*, 2013, 25: 061901
- 29 Winkler, R.G., Fedosov, D.A. and Gompper, G., *Curr. Opin. Colloid & Interface Sci.*, 2014, 19: 594

- 30 Zhao, H. and Shaqfeh, E.S.G., *J. Fluid Mech.*, 2013, 725: 709
- 31 Fedosov, D.A., Noguchi, H. and Gompper, G., *Biomech. Model Mechanobiol.*, 2014, 13: 239
- 32 McWhirter, J.L., Noguchi, H. and Gompper, G., *Soft Matter*, 2011, 7: 10967
- 33 McWhirter, J.L., Noguchi, H. and Gompper, G., *Proc. Natl. Acad. Sci. U.S.A.*, 2009, 106: 6039
- 34 Zhao, H. and Shaqfeh, E.S.G., *J. Fluid Mech.*, 2011, 674: 578
- 35 Lis, L.J., McAlister, M., Fuller, N., Rand, R.P. and Parsegian, V.A., *Biophys. J.*, 1982, 37: 657
- 36 Parsegian, V.A., *Annu. Rev. Biophys. Bioeng.*, 1973, 2: 221
- 37 Ramachandran, A., Anderson, T.H., Leal, L.G. and Israelachvili, J.N., *Langmuir*, 2010, 27: 59
- 38 Thomas, W.E., Trintchina, E., Forero, M., Vogel, V. and Sokurenko, E.V., *Cell*, 2002, 109: 913
- 39 Soddemann, T., Dünweg, B. and Kremer, K., *Phys. Rev. E*, 2003, 68: 046702
- 40 Hsu, W. and Chen, Y.L., *J. Chem. Phys.*, 2010, 133: 034906
- 41 Saric, A. and Cacciuto, A., *Soft Matter*, 2011, 7: 1874
- 42 Zhang, D., Chai, A., Wen, X., He, L., Zhang, L. and Liang, H., *Soft Matter*, 2012, 8: 2152
- 43 Chen, S., Phan-Thien, N., Khoo, B.C. and Fan, X.J., *Phys. Fluids*, 2006, 18: 103605
- 44 Fedosov, D.A., Peltomäki, M. and Gompper, G., *Soft Matter*, 2014, 10: 4258
- 45 Kikuchi, N., Pooley, C.M., Ryder, J.F. and Yeomans, J.M., *J. Chem. Phys.*, 2003, 119: 6388
- 46 Noguchi, H. and Gomper, G., *Phys. Rev. Lett.*, 2004, 93: 258102
- 47 Groot, R.D. and Warren, P.B., *J. Chem. Phys.*, 1997, 107: 4423
- 48 Yao, L., *Chinese J. Polym. Sci.*, 2015, 33(3): 465
- 49 Chai, A.H. and Zhang, L.X., *Chinese J. Polym. Sci.*, 2011, 29(6): 684
- 50 Plimpton, S.J., *J. Comput. Phys.*, 1995, 117: 1
- 51 Rudnick, J. and Gaspari, G., *J. Phys. A*, 1986, 19: L191
- 52 Zifferer, G., *J. Chem. Phys.*, 1995, 102: 3720
- 53 Su, J., Zhang, L. and Liang, H., *J. Chem. Phys.*, 2008, 129: 044905
- 54 Noguchi, H. and Yoshikawa, K., *J. Chem. Phys.*, 1998, 109: 5070
- 55 Keller, S.R. and Skalak, R., *J. Fluid Mech.*, 1982, 120: 27
- 56 Loan, H.N.P., Gooris, G.S. and Bouwstra, J.A., *J. Investigative Dermatology*, 2004, 123: 902
- 57 Landau, L.D. and Lifshitz, E.M., "Theory of elasticity", Pergamon: New York, 1970