Two-Dimensional Vesicle Hydrodynamics from Hydrophobic Attraction Potential

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We develop a new model, to our knowledge, for the many-body hydrodynamics of amphiphilic Janus particles suspended in a viscous background flow. The Janus particles interact through a hydrophobic attraction potential that leads to self-assembly into bilayer structures. We adopt an efficient integral equation method for solving the screened Laplace equation for hydrophobic attraction and for solving the mobility problem for hydrodynamic interactions. The integral equation formulation accurately captures both interactions for near touched boundaries. Under a linear shear flow, we observe the tank-treading deformation in a two-dimensional vesicle made of Janus particles. The results yield measurements of inter-monolayer friction, membrane permeability, and at large shear rates, membrane rupture. The simulations studies include a vesicle in parabolic flow and vesicle-vesicle interactions in shear and extensional flows. The hydrodynamics of the Janus particles vesicle replicate the behaviour of an inextensible elastic vesicle membrane.

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1. Introduction

Described by physicist Pierre-Gilles de Gennes as “another animal in soft matter physics”, the Janus particle—often a spherical particle with a hydrophobic and a hydrophilic hemisphere—exhibits complex aggregate, clustering, and self-assembly into mesoscopic and macroscopic structures that are relevant to a wide range of applications in biology and bioengineering.
Figure 1: Panel (a) illustrates the domain and boundary conditions for the mobility problem. The color map in panels (b)–(e) is the solution $u$ of (2.8). Red is for $u = 1$ and blue is for $u = 0$. Particles self-assemble into vesicle bilayers (panel (b)) and eventually align along inner and outer leaflets. In panel (c), $C_M$ is the midplane curve, $A$ is the enclosed area, and $L$ is the arc length. Initially stretched vesicles relax to equilibrium with fluid flow across the bilayer. The study considers a single vesicle in background flows such as shear flow (panel (d)) and hydrodynamic vesicle-vesicle interactions (panel (e)).

(de Gennes (1991)). Whether it is surface chemistry or polarity under an external field, the dynamics of Janus particles in a viscous solvent is inevitably the combination of long-range hydrodynamics interactions with both short- and intermediate-range particle-particle interactions. Such multi-scale nature of Janus particle dynamics underlies the richness of a Janus particle suspension, as de Gennes (1991) suggested by the example of a “thin film of Janus grains” that can breathe due to the interstices between Janus particles.

Recently, Fu et al. (2020) illustrated that the hydrophobic interactions between Janus particles (JP) in a viscous solvent can be used as a coarse-grained model to capture the mechanics of an elastic bilayer membrane of amphiphilic macromolecules such as lipids. Depending on their total number and geometry, JP suspensions can aggregate to form a micelle, a patch of bilayer membrane with open ends, and a self-enclosed bilayer membrane, referred to as a JP vesicle. Using a hybrid continuum model for the interactions between amphiphilic particles in a viscous solvent and with a boundary integral formulation, Fu et al. (2020) showed that the granularity of membrane remodeling, as occurs during fusion and fission of bilayers, can be accurately captured by the coarse-grained model.

In the present work, we extend the hybrid continuum model in Fu et al. (2020) for the Janus suspension to incorporate the collective hydrodynamics of a Janus suspension under various flows. The JP vesicles in our simulations replicate well-know vesicle hydrodynamics such as tank-treading and inter-leaflet slippage in a shear flow and migration in Poiseuille flow from continuum models. Furthermore we use the hybrid continuum model to investigate
permeability and rupture of a bilayer membrane due to an imposed flow. Finally, we compare a pair of interacting JP vesicles with a continuum model of a pair of vesicles.

Brandner et al. (2019) used the coarse-grained force field with a lattice Boltzmann molecular dynamics to simulate the hydrodynamics of a nano-sized vesicle under a shear flow. In MD simulations, the hydrodynamic interactions for the solvent phase are often approximated by an implicit solvent coarse-grained model. In the present work, the hydrodynamic interactions come from the mobility problem for the Stokes equations for the incompressible, viscous solvent.

We require a numerical method to avoid unphysical contact between rigid Janus particles. Optimization-based contact methods introduce constraints, such as enforcing a non-positive space-time interference volume (Lu et al. (2017); Bystricky et al. (2020); Yan et al. (2020)). These methods do not introduce stiffness, but do require solving potentially expensive nonlinear complementarity problems at each time step. Repulsion-based contact methods, which we employ, introduce an artificial repulsion force that increases in strength as two particles approach one another (Glowinski et al. (2001); Feng & Michaelides (2004); Kabacaoglu et al. (2018)). Strong repulsion forces can introduce numerical stiffness, but with the presence of the hydrophobic forces, we maintain contact-free suspensions with a relatively weak non-stiff repulsive force.

The paper is organized as follows. In §2 we present the formulation for the Janus particles in a viscous fluid in the zero-Reynolds number regime (Figure 1a). In § 3 we extend the hybrid continuum model for a Janus suspension to include the effects of a far-field flow via the mobility problem formulation. In §4 we validate our model and present simulation results for a single JP vesicle (Figure 1d) and for a pair of JP vesicles (Figure 1e) under various flowing conditions. Finally we provide discussion and outlook for future directions in § 5.

2. Governing Equations

2.1. Mobility Problem

The objective of this work is to study the hydrodynamics of JP vesicles in background flows. We consider an \( N_b \)-many body collection of JP suspended in a two-dimensional unbounded domain \( \Omega \). The boundary of each particle is denoted by \( \Gamma_i \) so that \( \partial \Omega = \Gamma_1 \cup \Gamma_2 \cup \cdots \cup \Gamma_{N_b} \) (Figure 1a). Assuming the inertial terms are negligible, the governing equations are

\[
-\mu \Delta u + \nabla p = 0, \quad x \in \Omega, \tag{2.1}
\]

\[
\nabla \cdot u = 0, \quad x \in \Omega, \tag{2.2}
\]

\[
u - u_\infty \to 0, \quad |x| \to \infty, \tag{2.3}
\]

where \( u \) is the velocity, \( p \) is the pressure, \( u_\infty \) is the background flow, and \( \mu \) is the constant viscosity. Since each particle \( \Gamma_i \) with centre \( a_i \) is a rigid body, its velocity satisfies

\[
v(x) = v_i + \omega_i (x - a_i)^\perp, \quad x \in \Gamma_i, \tag{2.4}
\]

where \( v_i \) is its translational velocity and \( \omega_i \) is its angular velocity. Here, \( \langle x, y \rangle^\perp = \langle -y, x \rangle \). Therefore, the no-slip boundary condition on each particle is

\[
u(x) = v_i + \omega_i (x - a_i)^\perp, \quad x \in \Gamma_i. \tag{2.5}
\]

To determine the translational and angular velocities of each particle, we define imposed forces \( F_i \) and torques \( T_i \) acting on each particle. Since the small particles are inertialess,
force and torque balance gives

\[ F_i - \int_{\Gamma_i} \sigma \cdot v \, ds = 0, \quad i = 1, \ldots, N_b, \]  
\[ T_i - \int_{\Gamma_i} (x - a_i) \cdot (\sigma \cdot v) \, ds = 0, \quad i = 1, \ldots, N_b, \]

where \( \sigma = -p I + \mu \left( \nabla u + \nabla u^T \right) \) is the hydrodynamic stress tensor (pressure tensor) and \( v_i \) is the particle outward normal. The process of finding the translational and angular velocities given the forces and torques is referred to as the mobility problem.

### 2.2. Imposed Forces

The imposed forces and torques contain two parts: hydrophobic attraction and repulsion. The hydrophobic attraction potential was introduced by Fu et al. (2020) and is responsible for forming particle aggregates that sequester their hydrophobic surface regions (Figure 1b). We model hydrophobic attraction by solving the screened Laplace equation boundary value problem

\[ -\rho^2 \Delta u + u = 0, \quad x \in \Omega, \]  
\[ u(x) = f_i(x), \quad x \in \Gamma_i, \quad i = 1, \ldots, N_b, \]  
\[ u \to 0, \quad |x| \to \infty, \]

where \( 0 \leq f_i \leq 1 \) is a material label with \( f_i = 0 \), respectively 1, representing hydrophilic, respectively hydrophobic, portions of the surface. We assume that both \( f_i \) and \( \Gamma_i \) are smooth. The parameter \( \rho > 0 \) is the decay length of attraction. The forces and torques of attraction are

\[ F_i^{\text{hydro}} = \int_{\Gamma_i} T \cdot v \, ds, \quad T_i^{\text{hydro}} = \int_{\Gamma_i} (x - a_i) \cdot (T \cdot v) \, ds, \]

where

\[ T = \gamma \rho^{-1} u^2 I + 2 \rho \gamma \left( \frac{1}{2} |\nabla u|^2 I - \nabla u \nabla u^T \right) \]

is the hydrophobic stress tensor and \( \gamma > 0 \) is the interfacial tension.

The second part of the imposed forces and torques comes from repulsion between proximal particles. Given a pair particles indexed with \( i \) and \( j \), we find the two points \( \tilde{x}_i \in \Gamma_i \) and \( \tilde{x}_j \in \Gamma_j \) that are closest to one another (Figure 1a). We then define the repulsion force and torque

\[ F_i^{\text{repul}} = \sum_{j \neq i} \frac{\tilde{x}_j - \tilde{x}_i}{|\tilde{x}_i - \tilde{x}_j|} P'(|\tilde{x}_i - \tilde{x}_j|), \]  
\[ T_i^{\text{repul}} = \sum_{j \neq i} \frac{(\tilde{x}_i - a_i) \cdot \tilde{x}_j}{|\tilde{x}_i - \tilde{x}_j|} \frac{\tilde{x}_i - \tilde{x}_j}{|\tilde{x}_i - \tilde{x}_j|} P'(|\tilde{x}_i - \tilde{x}_j|). \]

The repulsion profile \( P(r) \) is set to zero for distances \( r \) larger than a repulsion length scale \( \rho_0 \). As such, (2.13) and (2.14) ignore particles outside a \( \rho_0 \)-tubular neighborhood of \( \Gamma_i \). For \( 0 \leq r < \rho_0 \), we use \( P(r) = M (1 - \sin(r/r_0)) \) where \( M \) is sufficiently large to prevent particle collisions. Then, the total imposed force and torque are

\[ F_i = F_i^{\text{hydro}} + F_i^{\text{repul}}, \quad T_i = T_i^{\text{hydro}} + T_i^{\text{repul}}, \quad i = 1, \ldots, N_b. \]
2.3. Time Marching

By solving the mobility problem, we obtain translational and angular velocities of the $N_b$-body system. A second-order Adams-Bashforth scheme updates the particle positions and orientations. By including the repulsion force (2.13), particle collisions are avoided even when using a relatively large time step.

3. Integral Equation Method

Computing the hydrophobic attraction potential and the particle forces and torques requires the solution of elliptic partial differential equations (PDEs) in an unbounded complex domain. We recast both these PDEs as boundary integral equations (BIEs). We discretize each BIE at $N$ points on each of the $N_b$ particles with a collocation method. Integrals that are smooth are computed with the spectrally-accurate trapezoid rule, and nearly-singular integrals, caused by close contact between two particles, are computed with a high-order interpolation-based quadrature rule (Quaife & Biros (2014)). After discretizing and applying quadrature, the resulting linear system is solved with matrix-free GMRES, and we guarantee that the number of GMRES iterations is mesh-independent by using second-kind BIEs.

3.1. HAP Boundary Integral Equation

Similar to our previous work (Fu et al. (2020)), we represent the HAP as a double-layer potential

$$ u(x) = \frac{1}{2\pi} \int_{\partial\Omega} \frac{\partial}{\partial y} K_0 \left( \frac{|x-y|}{\rho} \right) \sigma(y) \, ds_y, \quad x \in \Omega, \quad (3.1) $$

where $K_0$ is the zeroth-order modified Bessel function of the first kind and the integral is taken in the sense of principle value whenever $x \in \partial\Omega$. By requiring that the density function $\sigma$ satisfies the second-kind integral equation

$$ f(x) = \frac{1}{2} \sigma(x) + \frac{1}{2\pi} \int_{\partial\Omega} \frac{\partial}{\partial y} K_0 \left( \frac{|x-y|}{\rho} \right) \sigma(y) \, ds_y, \quad x \in \partial\Omega, \quad (3.2) $$

the HAP double-layer potential (3.1) satisfies the screened Laplace equation (2.8)–(2.10). After discretizing (3.2), the result is an $NN_b \times NN_b$ linear system that is solved with block-diagonal preconditioned GMRES.

To calculate the hydrophobic force and torque, the gradient of the double-layer potential (3.1) must be computed on the boundary of each particle. The resulting integrands are singular, and specialized quadrature would be necessary to approximate such integrals. Alternatively, in Section 3.3, we show how the force and torque calculations can be expressed in terms of non-singular integrals.

3.2. Mobility Problem Boundary Integral Equation

Following previous work of Bystricky et al. (2020), we use the velocity representation of Power & Miranda (1987). In particular, we write the velocity as the sum of a double-layer potential and $N_b$-many Stokeslets and rotlets

$$ u(x) = u_\infty(x) + D[\eta](x) + \sum_{i=1}^{N_b} (S(x, a_i) F_i + R(x, a_i) T_i), \quad x \in \Omega. \quad (3.3) $$
The double-layer potential is

\[ D[\eta](x) = \frac{1}{\pi} \int_{\partial\Omega} \frac{r \cdot n \otimes r}{|r|^2} \eta(y) \, ds, \]  

(3.4)

where \( r = x - y \) and \( \rho = |r| \). The Stokeslet and rotlets centred at \( a_i \) are

\[ S(x, a_i)F_i = \frac{1}{4\pi} \left( -\log|r| + \frac{r \otimes r}{|r|^2} \right) F_i, \]  

(3.5)

\[ R(x, a_i)T_i = \frac{1}{4\pi} \frac{r^\perp}{|r|^2} T_i, \]  

(3.6)

respectively, where \( r = x - a_i \). The Stokeslet is torque-free and has force \( F_i \) while the rotlet is force-free and has torque \( T_i \). Therefore, the velocity (3.3) satisfies the total force (2.6) and torque (2.7) conditions if the double-layer potential \( D[\eta] \) is force- and torque-free. Matching the limit of (3.3) with the rigid-body motion, and imposing that \( D[\eta] \) is force- and torque-free, the density function \( \eta \), translational velocity \( v_i \), and angular velocity \( \omega_i \) satisfy

\[ v_i + \omega_i (x - a_i)^\perp = u_\infty(x) - \frac{1}{2} \eta(x) + D[\eta](x) \]  

\[ + \sum_{j=1}^{N_b} (S(x, a_j)F_j + R(x, a_j)T_j), \quad x \in \Gamma_i, \quad i = 1, \ldots, N_b, \]  

(3.7)

\[ \int_{\partial\Gamma_i} \eta \cdot v_i \, ds = 0, \quad i = 1, \ldots, N_b, \]  

(3.8)

\[ \int_{\partial\Gamma_i} \eta \times (x - a_i)^\perp \cdot v_i \, ds = 0, \quad i = 1, \ldots, N_b. \]  

(3.9)

After discretizing and applying appropriate quadrature rules, the result is a \((2NN_b+3N_b) \times (2NN_b+3N_b)\) linear system that we solve with block-diagonal preconditioned GMRES. Other BIE formulations of the mobility problem use single-layer potentials (Corona et al. (2017); Rachh & Greengard (2016)) or a combination of single- and double-layer potentials (Corona & Veerapaneni (2018)).

We have validated our solver for (3.7)–(3.9) using a single elliptical particle suspended in a background shear flow (see § 4.2.1). Hydrophobic attraction and repulsion are zero for a single particle (see Fu et al. (2020) equation 2.13). The angle of the ellipse’s major axis coming from the integral equation method agrees with the theoretical, Jeffery orbit time-course (Jeffery (1922)).

3.3. Main Theoretical Result: Calculating the Hydrophobic Force

Once (3.2) has been solved for \( \sigma \), we need to evaluate the integrals (2.11) which are the HAP forces and torques. These integrals involve the stress (2.12) which contains a singular integral for the gradient of the double-layer potential. To avoid singular integrals, we first define

\[ v_i(x) = u(x) - u_i(x), \]  

(3.10)

where

\[ u_i(x) = \frac{1}{2\pi} \int_{\Gamma_i} \frac{\partial}{\partial n_y} K_0 \left( \frac{|x - y|}{\rho} \right) \sigma(y) \, ds_y, \quad x \in \mathbb{R}^2. \]  

(3.11)

That is, \( v_i(x) \) is the double-layer potential (3.1) with \( \Gamma_i \) excluded from \( \partial\Omega \). Having defined \( v_i \), we prove
Theorem 1.

\[ F_i^\text{hydro} = \int_{\Gamma_i} J_i \, ds, \quad T_i^\text{hydro} = \int_{\Gamma_i} (x - a_i) \cdot J_i \, ds, \]  

(3.12)

where

\[ J_i = 2\gamma \rho^{-1} \sigma v_i + 2\gamma \rho \frac{d\sigma}{ds} v_i \cdot v - 2\gamma \rho \frac{d\sigma}{ds} \frac{dv_i}{d\gamma}. \]  

(3.13)

The symbols \( \tau \) and \( \frac{d}{ds} \) are the unit tangent and arc length derivative for \( \Gamma_i \), respectively. Using (3.12) over (2.11) is that the components \( \sigma, v_i, \frac{d\sigma}{ds}, \) and \( \frac{dv_i}{d\gamma} \) of \( J_i \) are smooth functions, whereas the components of (2.12) are singular integrals.

To prove (3.12), let

\[ T = S(u_i, u_i) + (S(u_i, v_i) + S(v_i, u_i)) + S(v_i, v_i) \]

\[ = T_1 + T_2 + T_3 \]

where we introduce the bilinear form

\[ S(u, v) = \gamma \rho^{-1}uvI + \gamma \rho \nabla v \cdot \nabla I - 2\gamma \rho \nabla v \nabla^T. \]  

(3.14)

Using the fact that \( u, u_i \), and \( v_i \) solve the screened Laplace equation (2.8), and that \( T, T_j, j = 1, 2, 3 \) are symmetric, it is straightforward to verify that

\[ \nabla \cdot T_j = 0, \quad \nabla \cdot ((x - a_i) \cdot T_j) = 0, \quad j = 1, 2, 3. \]  

(3.15)

Let \( U_i \) be the interior of the particle indexed by \( i \). For \( x \in \Gamma_i \) and an arbitrary function \( g(x) \), the notation

\[ [[g]](x_0) = \lim_{x \to x_0^+} g(x) - \lim_{x \to x_0^-} g(x), \]  

(3.16)

denotes the jump of the limits of \( g(x) \) taken from the outside to the inside of \( \Gamma_i \).

Lemma 1.

\[ F_i^\text{hydro} = \int_{\Gamma_i} [[T_2]v] \, ds, \quad T_i^\text{hydro} = \int_{\Gamma_i} (x - a_i)^\perp \cdot [[T_2]v] \, ds. \]  

(3.17)

Proof. To show (3.17), we expand (2.11) as

\[ F_i = \int_{\Gamma_i} T_1 v + T_2 v + T_3 v \, ds. \]  

(3.18)

By (3.10) and (3.15), we have that \( u_i \) is smooth and \( \nabla \cdot T_1 = 0 \) in \( \mathbb{R}^n \setminus U_i \). Similarly, \( v_i = u - u_i \) is smooth and \( \nabla \cdot T_3 = 0 \) in \( U_i \). By the divergence theorem,

\[ \int_{\Gamma_i} T_1 v \, ds = -\int_{\mathbb{R}^n \setminus U_i} \nabla \cdot T_1 \, dx = 0, \quad \int_{\Gamma_i} T_3 v \, ds = \int_{U_i} \nabla \cdot T_3 \, dx = 0. \]  

(3.19)

Finally, \( u_i \) and \( v_i \) are smooth and \( \nabla \cdot T_2 = 0 \) in \( U_i \). This gives

\[ 0 = \int_{U_i} \nabla \cdot T_2 \, dx = -\int_{\Gamma_i} (T_2 v)^- \, ds, \]  

(3.20)

where the superscript denotes the limit taken from in \( U_i \). Combining the above gives the first equation in (3.17). The argument for the second equation in (3.17) is identical. \( \square \)
t = 0 µs

(b)
t = 4 µs

Figure 2: JP vesicles undergo tank-treading in shear flow. In panel (a), the initial, 58-body vesicle is circular and the black arrows point in the direction of the hydrophobic side of the JP. In panel (b), the JP suspension rotates and deforms with the shear flow. The color map is for the solution of (2.8). The white curves are the streamlines of u. The shear rate is χ = 0.0025.

We have the following jump relations for (3.10):

\[
[[u_i]] = \sigma, \quad [[v_i]] = 0, \quad [[\nabla u_i]] = \frac{d\sigma}{ds}, \quad [[\nabla v_i]] = 0, \quad (3.21)
\]
on Γi (see, e.g. Klöckner et al. (2013)). Therefore,

\[
[[T_2 v]] = [[S(u_i, v_i) v + S(v_i, u_i) v]]
\]

\[
= [[(2\gamma \rho^{-1} u_i v_i I + 2\gamma \rho \nabla u_i \cdot \nabla v_i I - 2\gamma \rho \nabla u_i \nabla v_i^T - 2\gamma \rho \nabla v_i \nabla u_i^T ) v]]
\]

\[
= 2\gamma \rho^{-1} \sigma v_i v + 2\gamma \rho \frac{d\sigma}{ds} \frac{dv_i}{ds} v - 2\gamma \rho \frac{d\sigma}{ds} \frac{dv_i}{ds} \tau = J_i.
\]

Combining this with (3.17) gives (3.12) as required.

4. Numerical Results

4.1. Model Parameters

Fu et al. (2020) studied physical quantities for static JP vesicles for various particle shapes. In the present study, we fix the particle shape and vary the background flows. Specifically, the particles are circular disks with diameter \( l_0 = 2.5 \) nm. The boundary conditions (2.9) are \( f_i(x) = \frac{1}{2}(1 + \cos \theta_i) \) where \( \theta_i \) is the angle between \( x - a_i \) and \( d_i \), where the vectors \( a_i \) and \( d_i \) are the particle centre and director respectively. The particle diameter is the thickness of monolayers and the director points in the direction of the hydrophobic side of the JP.

We use \( \rho = 2l_0 \) for decay length, \( \rho_0 = 0.2l_0 \) for repulsion length, \( M = 4.0 \ k_B T \) for repulsion strength, \( \gamma = 4.1 \ \text{pN \ nm}^{-1} \) for interfacial tension, and \( \mu = 1 \ \text{cP} = 1 \ \text{pN ns nm}^{-2} \) for viscosity of room-temperature water. We nondimensionalize the problem through the change of variables \( t \mapsto t \) ns, \( x \mapsto x \) nm, \( u \mapsto u \) nm ns\(^{-1} \), and \( p \mapsto p \) pN nm\(^{-2} \). The numerical time step size is \( \Delta t = 0.2 \).

To reach consistent simulation outcomes, we first solve for a baseline JP vesicles that is suitably close to equilibrium. We start with an assumed configuration of \( N = 58 \) JP in the form of two, circular, apposing monolayers of about 8 nm in radius. The norms of the translational and rotational velocities vanish exponentially with an approximate decay rate
Figure 3: JP vesicles lose enclosed area but conserve length in a shear flow. Panel (a) gives the reduced area over time for four different shear rates. The monotonic curves are a two-exponential best fit. There is a commensurate increase in excess length (panel (b)), but the arc length of the mid plane curve is more or less constant for all shear rates (panel (c)). The inset in panel (c) is for shear rate 0.003. The legend in panel (b) applies to panels (a)–(c). Panel (d) plots the steady-state reduced area and the decay rate $k_2$ (inset) coming from the fitting data in panel (a).

An equilibrium configuration is therefore rapidly attained. This equilibrium configuration serves as the initial data in the subsequent background flow simulations.

4.2. Tank-Treading Vesicles

4.2.1. Vesicle in a Shear Flow

Our simulation studies begin by showing, for the first time, that a JP suspension with hydrophobic attraction behaves as a tank-treading vesicle (Finken et al. (2008); Zhao & Shaqfeh (2011)). The centroid of the baseline, 58-body JP vesicle lies at the origin and the background shear flow

$$\mathbf{u}(x) = \dot{\gamma}(x \cdot \mathbf{e}_x)\mathbf{e}_x,$$

is applied for shear rate $\dot{\gamma}$, and orthogonal unit vectors $\mathbf{e}_x$ and $\mathbf{e}_y$ for the horizontal and vertical directions, respectively. We use the dimensionless shear rate $\chi = \dot{\gamma} (s^{-1})$ ns.

Figure 2 shows snapshots of the JP vesicle in the shear flow with $\chi = 0.0025$. Under the
Figure 4: Inter-monolayer slip is present in the JP vesicle tank-treading motion at all shear rates. Panel (a) tracks a pair of particles (blue and yellow). The shear rate is $\chi = 0.005$ and in the right figure, the yellow particle will complete two and a quarter revolutions in the same time the blue particle completes two revolutions. The curves in panel (b) are the distance the outer leaflet has slid past the inner leaflet. The slopes of the curves give the slip velocity. With the exception of $\chi = 0.0035$, the slip velocity is generally monotonic in the shear rate.

background flow, the rigid-body boundary condition (2.5) causes the particle suspension to elongate. This perturbation disrupts the preferred particle orientations and exposes the hydrophobic core to bulk water (Figure 2, red region). In response, hydrophobic attraction (2.11) causes the particles to reorient and form a somewhat elliptically-shaped suspension. Panel (a) shows the initial configuration and panel (b) shows the later, fully-formed, clockwise tank-treading motion. The JP suspension maintains its bilayer structure throughout the simulation.

To extract physical quantities, let $A^* = 4\pi A / L^2$ be the reduced area and $\Delta = L / \sqrt{A/\pi} - 2\pi$ the excess length of the bilayer structure (Finken et al. (2008)). Here, $A$ is the enclosed area and $L$ is the total length of the JP vesicle (Figure 1a). Figure 3 shows the evolution of the area and length for various shear rates. Panels (a) and (b) show that $A^*$ decreases and $\Delta$ increases with time, respectively, and that the rate of decrease/increase grows with shear rate. The total arc length, however, remains constant for all time for all four shear rates (panel (c)). We conclude that the JP vesicle loses area and that the bilayer behaves as a permeable membrane.

Since the starting configuration is nearly circular, the reduced area decreases from an initial value close to 1 and tends to a steady-state value $A^*_{\infty}$. The data in panel (a) are fit to the model $A^* = (A^*_{\infty} - a_1 - a_2) + a_1 \exp(-k_1 t) + a_2 \exp(-k_2 t)$, $0 < k_2 < k_1$. Panel (d) shows that $A^*_{\infty}$ decreases with the shear rate. The JP vesicle achieves a steady-state reduced area
Table 1: Friction Coefficients

| \( \dot{\gamma} \) (ns\(^{-1}\)) | 0.0020 | 0.0025 | 0.0030 | 0.0035 | 0.0040 | 0.0045 | 0.0050 |
|---|---|---|---|---|---|---|---|
| \( b \) (pN ns nm\(^{-3}\)) | 0.43 | 1.19 | 0.42 | 0.69 | 0.97 | 0.80 | 1.07 |

earlier when the shear rate is low (inset), but the decay rate \( k_2 \) is more or less constant for higher shear rates.

The oscillations in the data of Figure 3 are due to the granularity of the JP vesicle. The inset of Figure 3c zooms in on the arc length data for the shear rate \( \chi = 0.003 \). It shows that the oscillations are smooth and well-resolved by our second-order Adams-Bashforth scheme.

We point out that the range of values for \( \chi \) where we measured for tank-treading correspond to shear rates \( \dot{\gamma} = O(10^6 \text{ s}^{-1}) \) which gives fluid velocities \( O(10^6 \text{ m s}^{-1}) \) in the vicinity of the vesicle. While large, these orders of magnitude are identical to ones used in prior MD studies (Brandner et al. (2019)) and are a consequence of the fact that larger shear rates are required to produce the viscous stresses needed to appreciably deform smaller vesicles.

4.2.2. Inter-Monolayer Friction

We observe inter-monolayer slip in the tank-treading, JP vesicle at all shear rates. Since they are not bound, the two leaflets of the vesicle are able to slide past one another. Monolayer slip effects have been incorporated in continuum models (Schwalbe et al. (2010)). In the present setting, slip is limited by viscous friction of the aqueous gaps between particles and by the constant unbinding and binding of particles pairs in apposing leaflets.

Figure 4a illustrates inter-monolayer slip by tracking the distances traveled by a pair of particles along the midplane curve. In the left image, the blue and yellow particle lie next to each other. In the right-most panel, the yellow particle has traveled farther than the blue particle. This suggests that the outer tangential velocity, obtained by projecting the velocity of the outer leaflet onto the midplane curve, is larger than that of the inner leaflet.

From the data, we obtain an inter-monolayer friction coefficient

\[
b = \frac{\langle F \rangle}{\langle L U \rangle},
\]

where \( F \) is the tangential force jump, \( L \) is the length of the midplane \( C_M \) (Figure 4a), and \( U \) is the slip velocity. The time average \( \langle \cdot \rangle \) is necessary to avoid division by zero whenever slip velocity vanishes.

The tangential force jump \( F \) equals the tangential shear force on the outer leaflet minus the tangential shear force on the inner leaflet. To calculate \( F \), we first let

\[
F_h = \int_{C_M^+} \tau \cdot \sigma \cdot v \, ds - \int_{C_M^-} \tau \cdot \sigma \cdot v \, ds \tag{4.3}
\]

where \( C_M^+ \) and \( C_M^- \) are target curves obtained by projecting the midplane curve \( C_M \) a distance \( h \) outward, respectively inward, along its unit normal vector field (Figure 4a). We sample \( F_h \) for \( h = \pm 1.3, \pm 1.5, \pm 1.7, \pm 1.9 \) times the particle radius and define \( F \) by extrapolating to zero distance. This avoids integrating along a curve passing directly through the particles.

To calculate \( U \), we let \( u_+(x) \) and \( u_-(x) \) be the tangential velocity of the outer, respectively
inner, leaflet. Then

\[ U = \frac{1}{L} \int_{C_M} u_+(x)(1 - \delta \kappa) - v_-(x)(1 + \delta \kappa) \, ds, \]  

(4.4)

where \( \delta \) is the distance from the leaflet centres to the midplane and \( \kappa \) is the curvature. The factors \( \pm \delta \kappa \) are needed to project the leaflet velocities, defined on the particle centres, onto the midplane curve. Finally, the function \( s(t) = \int_0^t dU \) records the distance one leaflet has slid past the other. Figure 4b plots the sliding distance for various shear rates.

Table 1 provides \( b = 0.79 \pm 0.3 \) pN ns nm\(^{-3}\) over a range of shear rates which is in good quantitative agreement with values previously reported in the literature. Atomistic studies have also considered inter-monolayer slip in lipid bilayers. Wohlert & Edholm (2006) and den Otter & Shkulipa (2007) reported \( b = 0.7 \times 10^6 \) Pa m\(^{-1}\) s = 0.7 pN ns nm\(^{-3}\) and \( b = 2.4 \) pN ns nm\(^{-3}\) for DPPC membranes simulated by MD, respectively. Using a more recent version of the Martini force field, Zgorski \textit{et al.} (2019) gives \( b = 5.5 \) pN ns nm\(^{-3}\) for shear rates 0.4 ns\(^{-1}\) and higher. It is understandable that there is uncertainty in the friction coefficients of Table 1. The scatter in our data, however, is fully consistent with that calculated from MD simulations, c.f. the transient rise in values of Table 1 and in Zgorski \textit{et al.} (2019), Figure 10 for low shear rates.

4.2.3. \textit{Membrane Ruptures}

A temporary fissure or a complete membrane rupture can occur at large shear rates. Figure 5 demonstrates how a vesicle can rupture when suspended in a shear flow. For \( \chi = 0.1 \), starting with a circular shape (Figure 5a), the vesicle is stretched by the background flow and fissures appear in the bilayer structure in multiple locations (Figure 5b). In Figure 5c, the ruptured vesicles form two planar micelles which are eventually carried off by the flow (Figure 5d).
4.2.4. Vesicle in a Parabolic Flow

Finally, we consider the parabolic background flow

$$\mathbf{u}_\infty = v_{\text{max}} \left[ 1 - \left( \frac{\mathbf{x} \cdot \mathbf{e}_y}{wR_0} \right)^2 \right] \mathbf{e}_x,$$

where $v_{\text{max}}$ is the flow strength and $w$ determines the shape of the flow. The parameter $R_0$ is the radius of the JP vesicle at $t = 0$ and $w$ sets the width of the profile. Kaoui et al. (2009); Coupier et al. (2008); Danker et al. (2009) have shown that the behaviour of a vesicle in this unbounded flow includes vertical migration, and depending on the flow rate and reduced area, the steady-state shape can be either a symmetric parachute or an asymmetric slipper.

Figure 6 shows four configurations for one specific case where the centroid of the JP vesicle is initially placed slightly above the $x$-axis. We have marked a pair of particles blue and yellow in the inner and outer leaflets, respectively, and observe that the deformed JP vesicle (Figure 6, $t = 12$ $\mu$s) has a counterclockwise movement and the shape of the vesicle approaches an asymmetric slipper shape. For this test, the reduced area in the final configuration is approximately 0.9 which matches the previous numerical tests in Kaoui et al. (2009) where a slipper-like shape occurs when the flow velocity is weak and the reduced area is large. The flow causes the vesicle, which is initially placed above the axis, to drift downward where it reaches a steady height of about 1 nm.

4.3. Stretching and Permeability

Finally, we show that the JP vesicle behaves as a permeable membrane and the inextensibility comes about due to a large stretching modulus. Figures 7b shows an initial, non-equilibrium JP vesicle suspended in a quiescent flow $\mathbf{u}_\infty = 0$. The color map plots the pressure $p$. The red color in Figures 7b shows a spatially constant, positive internal pressure (0.05 pN nm$^{-2}$) and the white shows a spatially constant zero, external pressure. There is some fluid flow and the pressure vanishes as the configuration tends toward the equilibrium state (Figures 7c).

What could be the source of this drop in pressure? In membrane continuum mechanics, small changes in surface area give rise to a membrane tension $\tilde{\gamma} = K_A(A/A_0 - 1)$ where
Figure 7: In JP vesicles, tension and pressure relax as fluid is expelled through the particle interstices. In panel (a), the thin curve plots the mean of the norm of the particle translational velocities. The thick curve plots the mean of the absolute value of the particle angular velocities. At $t = 0$ µs, the vesicle has a spatially constant internal pressure 0.05 pN nm$^{-2}$ (red color, panel (b)). In panel (c), pressure has dissipated and the vesicle has moved from its initial configuration (gray circles), to the equilibrium configuration (black circles). The data in panels (d) and (e) support the linear relationship expressed by (4.7) and (4.8). Circles are for a vesicle with 17 nm initial radius; square are for a 34 nm initial radius. Asterisks are for a 18 nm initial radius but with smaller, 1.25 nm diameter particles. In panel (f), the theoretical time course (4.9) overlaps the data using constants $K_A$ and $P$ derived from panels (d) and (e).

$A$ is the membrane surface area and $A_0$ is the reference surface area. The area modulus $K_A$ of bilayers is about 240 pN nm$^{-1}$ (Nagle & Tristram-Nagle (2000)). In the two-dimensional vesicles, the tension becomes

$$\tilde{\gamma} = K_A \left( \frac{L}{L_0} - 1 \right),$$

(4.6)

where $L$ and $L_0$ are the vesicle arc length and resting length, respectively. Moreover, stretched, circular vesicles has a Laplace pressure

$$\Delta p = \frac{\tilde{\gamma}}{R},$$

(4.7)

where $\Delta p$ is the difference in internal pressure to the pressure at infinity and $R^{-1}$ is the total curvature of the circular cylinder.

Figure 7c plots the data for the pressure jump $\Delta p$ between the particle centre and the far-field (see Figures 7c and 7d). We use $R = L/(2\pi)$ for the vesicle radius, and the horizontal axis is the relative stretch. The circles are data for a vesicle with radius 17 nm. The linear fit (solid lines) shows that $R\Delta p$ is proportional to the relative stretching $L/L_0 - 1$. The squares are for a vesicle with twice the radius 34 nm, and the data overlap supports that the proportionality constant $K_A$ is a stretching modulus that is independent of vesicle size. The data give $K_A = 170\pm9$ pN nm$^{-1}$ which is in good agreement with the experimentally obtained
Figure 8: Two JP vesicles suspended in a shear flow interact by orbiting about the origin. The moving paths of the two centroids are plotted in blue and red. The centroids are initially located on the x-axis. The fluid velocity streamlines appear in grey. The dimensionless shear rate is $\chi = 0.005$.

The area moduli of lipid bilayer. The reason the tank-treading vesicle appears inextensible ($L$ is more or less constant in Figure 3c) is because the modulus $K_A$ is large. To evaluate how changes to particle size lead to different physical properties, the asterisk symbols are for an 18 nm radius vesicle consisting of particles with diameter 1.25 nm, instead of the usual 2.5 nm. These data give a smaller stretching modulus of $K_A = 102 \text{ pN nm}^{-1}$.

The particles in our setup do not abut but rather have small gaps due to repulsive forces. The gaps allow for some fluid flux across the JP bilayer, and in membrane mechanics aqueous flux is quantified by the equation

$$\frac{dA}{dt} = -PL\Delta p,$$

where $P$ is a hydraulic permeability constant (Chabanon et al. (2017); Quaife et al. (2021)). Figure 7e shows that the data for $L\Delta p$ and $dA/dt$ obey the linear relationship expressed by (4.8). The slopes of the linear fits give the hydraulic permeabilities $P = 0.0296 \text{ nm}^3 \text{ ns}^{-1} \text{ pN}^{-1}$ and $P = 0.0283 \text{ nm}^3 \text{ ns}^{-1} \text{ pN}^{-1}$ for the 17 nm and 34 nm radius cases, respectively. Like the area modulus, the data give a permeability that is independent of vesicle size.

The hydraulic permeability we calculate, however, is not in agreement with experimentally derived values and is larger by a few orders of magnitude. We suspect this discrepancy is due to inter-particle distance of the JP being large compared to the inter-lipid spacing in real bilayers. To test this, we calculate the permeability for the particles with diameter 1.25 nm. Due to their smaller size but fixed repulsion strength, these particles have a larger inter-particle spacing resulting in an increase in permeability, $P = 0.0566 \text{ nm}^3 \text{ ns}^{-1} \text{ pN}^{-1}$ (Figure 7e, asterisk symbols).

Since the vesicles in Figure 7a are nearly circular, we can combine (4.6), (4.7), and (4.8), to derive

$$L_0(L - L(0)) + L_0^2 \ln \left| \frac{L - L_0}{L(0) - L_0} \right| = -4\pi^2 P K_A t.$$
Figure 9: The figure is for the same simulation as in Figure 8, but also plots the fluid pressure $p$. The color bar is identical for all panels. Internal pressure is initially zero, but then grows as the vesicles come close to contact (panel (c)). The insets are generated from simulations of a continuum model of the vesicles (Quaife et al. (2019)). The streamlines of the two models are in agreement.

All in all, the theoretical time courses for (4.9) are in good quantitative agreement with the JP data (Figure 7f).

4.4. Two Vesicles in a Linear Flow

4.4.1. Shear Flow

Finally, we can study vesicle-vesicle interactions in background flows. Figure 8 shows the simulation of two JP vesicles suspended in a shear flow with shear rate $\chi = 0.005$. We duplicate the pre-relaxed 58-body JP vesicle from previous sections and construct the initial configuration shown in Figure 8a. The two centroids are at coordinates $(-25, 0)$ and $(25, 0)$ in nm. In all panels, the blue and red curves show the trajectory of the two JP vesicle centroids. They have nearly completed a full period by $t = 4 \mu$s.

We show snapshots of the fluid pressure in Figure 9. Since the initial JP vesicles are pre-relaxed, there is initially no pressure jump between the internal and external fluids (panel (a)). Panels (b)–(d) show the configurations when $t = \{0.5, 1, 1.5\} \mu$s, and the streamlines are plotted in the background for all panels. We include the numerical results from a continuum model in all insets and these comparisons give a qualitative agreement between two models. We also observe an adhesive effect between the two JP vesicles that is set up by the hydrophobic attraction (Figure 9c). Similar dynamics have been observed between a pair
Figure 10: The initial placement of two JP vesicles suspended in an extensional flow affects the long-time dynamics. The moving paths of the two centroids are plotted in blue in red. Each row corresponds to a different initial placement of the JP vesicles. (i) Both JP vesicle centroids are on the x-axis. (ii) The centroid of the left JP vesicle is 0.25 nm above the x-axis and the right JP vesicle is on the x-axis. (iii) The centroid of the left JP vesicle is 0.25 nm above the x-axis and the right JP vesicle is 0.25 nm below the x-axis. (iv) The centroid of the left JP vesicle is 1.25 nm above the x-axis and the centroid of the right JP vesicle is 1.25 nm below the x-axis. The streamlines appear in grey and the flow rate is \( \dot{\gamma} = 0.005 \text{ ns}^{-1} \) in all cases.

of adhering vesicles in a shear flow (Quaife et al. (2019); Abbasi et al. (2021)). This adhesive behaviour is absent when two JP vesicles are well-separated.

4.4.2. Extensional Flow

Using a similar setup to the shear flow case, we suspend the same two, pre-relaxed, 58-body JP vesicles and consider their dynamics in an extensional flow

\[
\mathbf{u}_\infty(x) = \dot{\gamma} ((e_x \cdot x)e_x - (e_y \cdot x)e_y)
\]

(4.10)

with extensional rate \( \dot{\gamma} = 0.005 \text{ ns}^{-1} \). This extensional flow is stretching in the y-direction and squeezing in the x-direction. Figure 10 shows how the initial placement of the JP vesicles affects the dynamics. When two centroids are both placed symmetrically on the x-axis (case (i)), the JP vesicles come into contact and reach a steady equilibrium. If one centroid is placed
above the $x$-axis (case (ii)), the two JP vesicle move together and then upward. The migration of the right JP vesicle is a consequence of the adhesive effect caused by the hydrophobic interactions. When the two centroids start on opposite sides of the $x$-axis (case (iii)), they eventually diverge from one another along the $\pm y$-directions. Finally, when the two centroids start on opposite sides of the $x$-axis, but with a greater displacement (case (iv)), the JP vesicles move much faster along the $\pm y$-directions.

Figure 11 shows numerical results when the centroids of the two Janus particles are placed at $(-10, -0.1)$ nm and $(10, 0.1)$ nm (case (iii) from Figure 10). With this setup, the two JP vesicles eventually separate along the $\pm y$-directions and we compare the results against a continuum model as shown in all insets. Panels (b)–(d) show the transient behaviour of the JP vesicles and the continuum vesicles under an extensional flow. In both the coarse-grained model and the continuum model, the vesicles initially converge towards one other and then diverge along the $y$-axis. The behaviour of the streamlines in both cases are similar. The pressure is initially largest in the gap formed by two JP vesicles and decreases during the separation. The short-range repulsion plays an important role to avoid particle collisions.
5. Conclusion

Fu et al. (2020) developed a mathematical model to quantify the macroscopic assembly and mechanics of a JP vesicle in a viscous solvent. The interactions between JP are formulated as a second-kind integral equation, which is coupled to the Stokes equations for the surrounding incompressible fluid at the zero-Reynolds-number limit. Numerical simulations of a JP suspensions revealed self-assembly of JP into micelles and bilayers, providing an alternative means for computing mechanical moduli, which often requires the knowledge of an equation of state from experiments on a colloidal membrane (Balchunas et al. (2019)). Results in this work show great potential to study Janus colloids (Bradley et al. (2017); Mallory et al. (2017)) and the morphology of colloid surfactants (Bradley et al. (2016)). For example, with the flexibility of the model, we can specify the boundary condition on JP surfaces based on the chemicals used in experiments.

In the present study, we used this integral formulation and numerical algorithm to simulate the hydrodynamics of JP vesicles in background flows. Under a linear shear flow, we found a JP vesicle to exhibit elongation and tank-treading dynamics observed for a lipid bilayer GUV. The results showed that the reduced area $A^*$ decreases with shear rate but that the total length of a JP vesicle is conserved. The decay rate of the reduced area was independent of the shear rate values between 0.003 ns$^{-1}$ and 0.005 ns$^{-1}$. Moreover, the proposed model describes membrane rupture in high shear rates. Therefore, our method can be applied to vesicles undergoing topological changes which is difficult to simulate when using a continuum model that represents vesicles as closed and continuous curves.

We estimated the inter-monolayer friction $b$, membrane permeability constant $P$, and the membrane stretching modulus $K_A$. The inter-monolayer friction coefficient was determined by calculating the tangential shear force and slip velocities with respect to the bilayer mid-plane. The range of friction coefficients agree with values reported by den Otter & Shkulipa (2007) in their MD study. The coarse-graining level of the JP vesicle has a larger length scale than molecular dynamics simulations, and in the future convergence studies we will investigate how physical properties like the friction coefficient and membrane permeability depend on the particle shape and size.

We also simulate the spatial migration of a JP vesicle in a parabolic shear flow. Replicating the hydrodynamics of a GUV in a Poiseuille flow (Kaoui et al. (2009); Danker et al. (2009); Coupier et al. (2008)), the JP vesicle moves toward the centre of the shear flow. While the initial reduced area of the JP vesicle is $A^* \approx 1$, the equilibrium reduced area is $A^* = 0.9$. For the parameters we used in the simulation, the JP vesicle takes on an asymmetric, “slipper” shape as it settles above the centre of flow and exhibits tank-treading motion. An interesting result contrast with continuum results is that the JP vesicle oscillates at a height slightly above the centre of the Poiseuille flow.

We further simulated the hydrodynamics of two JP vesicles, and drew comparisons with simulation results of two vesicles described by the Helfrich continuum model. A comparison of the vesicle shapes and the streamlines demonstrate remarkable similarities. The two overlapping trajectories of the JP vesicles’ centroids in a shear flow evolve as expected when the two centroids are initialized on the same horizontal level. We also observe a rotating behaviour that is observed for models involving vesicle adhesion (Quaife et al. (2019)). The hydrophobic attraction led to this adhesive effect when two JP bilayers are sufficiently close. We also performed several simulations of a pair of JP vesicles suspended in an extensional flow. By varying the initial vertical displacement of the vesicles’ centroids, we can control for divergent trajectories and obtain similar results to the continuum model.

In § 3.3, we derived an alternative integral form for calculating the force and torque to avoid the singular integral evaluation. These alternative integrals allow us to accurately
resolve trajectories over long times without having to rely on computationally expensive quadratures.

Our future goals include extending the current framework to a three-dimensional JP vesicle system. This will require additional algorithmic implementation including a fast summation method such as the fast multipole method. Another research direction is to include the fluctuating hydrodynamics for Brownian suspensions (Bao et al. (2018)), and this is critical to understand membrane diffusion. Finally, a more physical boundary conditions for the HAP model will allow us to draw comparisons between computational and laboratory experiments.

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