Short summary of the paper:

In this paper, Fu *et al.* investigate the dynamics of vesicle-like assemblies of amphiphilic Janus particles (JP) suspended in 2D Stokes flow. They solve the integral formulation of the Stokes problem for the flow and the Laplace problem for the hydrophobic interaction potential. Their calculation of the hydrophobic forces and torques avoids evaluating singular integrals or to resort to complex methods such as quadrature by expansion. They use their numerical tool to study the dynamics of a single and a pair of self-assembled vesicular structures in a shear flow, in a parabolic flow and in an extensional flow. They show that these coarse-grained vesicles behave similarly to continuum models. They also characterize their constitutive parameters such as the inter-monolayer friction coefficient, the stretching modulus or the hydraulic permeability.

Recommendation:

Overall, the paper is original and interesting. The derivation of the hydrophobic force without singular integrals is smart and well written. The characterization of the effective properties of the coarse-grained vesicles is also of interest and carefully conducted. However, in many instances the manuscript looks more like a catalogue of the different behaviors JP vesicles can exhibit in linear flows, rather than a comprehensive study. The authors describe a few interesting phenomena but only partially address the exciting physical questions related to them. The paper lacks quantitative comparisons with continuum models, parametric studies and detailed explanations to meet the standards of JFM. In addition, the manuscript seems to have been written in haste: a figure with no apparent connection to the content of the paper has been inserted without being referenced or discussed in the text (see below), some parts need some serious proofreading and additional clarifications.

Below is the list of major and minor comments that need to be addressed before I can recommend publication of the manuscript in JFM.

Major comments/questions:

- There is no parametric study of the effect of the particle size on the effective properties of the vesicles (interlayer friction, stretching modulus, permeability,etc...). The authors defer this part for future work in the conclusions, but since the effect of the particle size is important, as evidenced in Section 4.3, it should be explored and explained more thoroughly in the manuscript, otherwise the research would be too incremental. The effect of particle shape seems indeed more complex and out of the scope of the current paper.
- The membrane rupture situation, briefly illustrated in Section 4.2.3, is not investigated at all. Is there a dimensionless number related to this phenomenon with a critical value above which rupture happens ? (e.g. quantifying the competition between shear and attraction)
- I understand that the results of Section 4.4 are mostly qualitative and that the goal is to show the visual agreement between the coarse-grained and continuum vesicle models, but it would be insightful to provide quantitative comparisons to measure how close they are to each other.
- The problem is not nondimensionalized with the characteristic scales of the system but with ns, nm and pN$\cdot$nm^{-2}. This (unusual) nondimensionalization makes it hard to compare physical quantities and to define order parameters that would explain/characterize some phenomena observed in the simulations (e.g. the membrane rupture).
- For the sake of clarity, at the end of Section 3 the authors should summarize the exact set of equations they use and the unknowns they solve for.

Minor comments/questions:

- General comment for all the figures with colormaps: it would be good to use colorblind friendly colormaps for colorblind people and for black and white printing.

- Figure 1: the arc length L does not appear in panel (c).
- Line 50: typo: "well-know**n**"
- Page 3: the first two paragraphs seem to be a bit disconnected from the rest of the introduction. Maybe the authors should rewrite that part so that there is a transition from the physical problem into consideration to the various numerical methods used in the literature to simulate it.
- Line 70: "we maintain contact-free suspensions with a relatively weak non-stiff repulsive force". What do you mean by relatively weak repulsive force ? Weak compared to what ? (see additional question on this hereinafter).
- Equation (2.4) is not necessary as the no-slip boundary condition is standard and it is redundant with (2.5).
- Section 2.2: for clarity, define the variable u as the hydrophobic attraction potential in the first paragraph.
- The equations of the continuous time evolution of the particle positions and orientations should be written in Section 2 to close the problem.
- I think the time-discretization Section 2.3 should go at the end of Section 3 since this is the one devoted to the numerical discretization of the governing equations. Also, the sentence "particle collisions are avoided even when using a relatively large time step" is very vague. What do you mean by "relatively large time step" ? Compared to what time scale ?
- Section 3: the acronym HAP is not defined in the text.
- Equation 3.1: use parenthesis to show that the normal derivative only applies to the Laplace's Green function K_0 and not the density σ.
- For clarity, use contraction products "$\cdot$" when a second order tensor multiplies a vector to avoid confusion (e.g. $\mathbf{S} \cdot \mathbf{F}$ instead of $\mathbf{SF}$) in eqs. (3.4), (3.5), (3.7) and so on...
- In practice, how do you compute the derivatives $d\sigma/ds$, dv_i/ds and $dv_i/d\boldsymbol{\nu}$ in (3.13) ?
- Line 256: you set the strength of the repulsive force $M = 4k_BT$. In your simulations there is no thermal fluctuations, so why using k_BT as a reference energy if it is no there in the simulations ? There should be another energy scale that you could use to calibrate M, right ?
- Related question: how much does the interparticle distance depend on on the strength and range of this artificial repulsive potential ? What is the impact on the vesicle shape and effective properties ?
- Figure 3a,b,d: what does the term in parenthesis "(1)" means on the label of the ordinate axis ?
- Line 302: the authors mention that tank-threading can only be observed for shear rate as high as $10^6\mathrm{s}^{-1}$. Can such a high value be generated in experiments ?
- Eq. 4.4, typo: $v_{\text{-}}$ should be $u_{\text{-}}$.
- Figure 6: the yellow particle is not visible when printing in black and white.
- Line 388, typo: "has" should be "**have**".
- Figure 7a is never referred to and its content is never discussed in the text.
- Line 393: The reference to panel "Figure 7c" seems to be a typo. Same for "Figures 7c and 7d" on line 394, I think it should be "Figures 7b and 7c".
- Side question: Is it possible to change the vesicle stretching modulus and hydraulic permeability independently or are these two properties linked to each other and how ?

- Line 421, typo: in “Since the vesicles in Figure 7a...”. Fig 7a is the velocity plot that is never discussed in the text.
- Line 481: acronym GUV is never defined in the text.
- Line 505: for the first time in the text the authors write that their continuum model for the vesicle is the Helfrich continuum model. This model, and the value of the parameters chosen for the comparisons with the coarse grained simulations, should at least be described in an appendix and referenced earlier in the text.
- It would be nice to have SI movies showing the various phenomena illustrated in the paper.