

High-volume fraction of simulations of two-dimensional vesicle suspensions

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The authors advance their two-dimensional boundary integral method for dense vesicle suspensions. In particular, they have added (1) a means of implicit time integration when the vesicles are closely placed. This is well understood to be a problem and their resolution is nice contribution. They also nicely analyze their (2) nearly-singular integration approach and include a (3) nifty collision detection component. The example simulations are well motivated and explained. They well demonstrate the method. I anticipate that others will draw on these advances. I do have some serious concerns that should be addressed, though I anticipate that the authors will be able to relatively easily address them before publication.

- Citation: the authors cite their 2010 paper for much of the background material. This has several problems:
 - There are extensive simulations of high-volume fraction configurations in two dimensions (Pozrikidis, Freund, Higdon), some of which have use spectral methods. The authors even go so far as to presume that their methods “will enable simulations with concentrated suspensions.” This blatantly denies the studies that others have already done this.
 - This fails to appreciate that there have also been extensive successful simulations of vesicle suspensions even in three dimensions (Shaqfeh, Graham, Freund).
 - With the citations listed, the authors seem to credit themselves for development of the Stokes-flow boundary integral formulation and fundamental phenomenology such as tank treading of the vesicle membrane.
 - Others have used near-singular formulations for vesicle simulations (Higdon, Zhao).
 - Others have developed time-implicit methods (Zhao, Dimitrakopoulos).

The authors make some genuine contributions, but the omission of the literature is unacceptable. (It actually would be possible to view this very negatively, but I choose not to. With a superficial read, a referee could easily say “Implicit and nearly singular have been done before and these authors are working on 2d when state-of-the-art is 3d. These

authors just don't know the literature." I do hope this is not actually the case!) This is my biggest concern, and this paper should not be published unless this is fully fixed. Fortunately, it is easy to correct.

- Given that so many others are already doing effective simulations in three dimensions, this extension needs to be addressed more completely. Extension to three-dimensions should be discussed more explicitly after the present formulation is presented.
- Page 5: \mathbf{f} seems to be a linearized constitutive model. How important is this for the implicit scheme? This must be addressed, especially since others have done so many successful simulations (including implicit) with significantly nonlinear finite-deformation constitutive models.
- Page 6: in 2d, others have removed the singularity and treated it analytically. Why isn't this done here? It would seem to then provide spectral accuracy. The remaining sharpish though C^∞ integrand could then be treated spectrally with the present method. (I do not think, however, that this would extend to three dimensions.)
- Relatively minor points:
 - Before (1): γ_p seems to be introduced prematurely
 - It would be good to state from the outset that collision detection is only needed to counteract numerical errors. Physical collisions should not occur in the Stokes limit.
 - Page 3. $f(\mathbf{x}) = [T]\mathbf{n}$ does not seem to be well formed. Is f a stress or a force, vector or rank-2 tensor, ...?
 - Equation (2): Δ is some sort of vector Laplacian? It's not a usual scalar Laplacian. I personally prefer $\mu \nabla \cdot (\nabla \mathbf{u} + (\nabla \mathbf{u})^T)$, but this is not a big deal.
 - Equation (2): The authors seem to use both σ and T for stress.
 - Page 4: The definition of Γ_0 is unclear/ill-formed.
 - Definition of \mathcal{S}_{pq} : " $-\mathbf{I} \log \rho$ " would be more clear.
 - Are we sure there is no 4 in front of the π in the definition of \mathcal{D}_{pq} ?
 - Page 5: " ω_1 is the interior of vesicle q ". This must be misrepresented.
 - Page 5: ν_p is repeatedly defined

- Page 5: what is meant by “hydrodynamic density”? Is this the local surface traction density?
- Page 6: “fully decoupled” should be explained more explicitly. Clearly, it is not literally true for the physical system.
- Page 7: “Then number of GMRES....”
- Footnote 3: This is usually presented as a dynamic condition based upon the lubrication limit of the flow equations. I do not think that the streamline condition can sufficiently explain evolution in time. (By their argument nothing should ever contact if separated by an incompressible continuum, but that failed to appreciate the dynamics associated with that continuum, which must be viscous, I think.)
- Section 5. I find the use of area and length to be acceptable in assessing performance, but the authors should more explicitly explain that these are dominated by relatively low-order moments of the shape and therefore very easy to compute accurately. I request that convergence of some harder quantity be added, at least for one example, though it will be less definitive without an exact solution. I would really like to know how the wall-vesicle distance converges for the stenosis.
- Stenosis: what is the exact shape of the wall used. It’s also unclear how the flow is imposed. This should be explained in detail.