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A coupled hybrid continuum-coarse-grained RBC membrane model

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ABSTRACT: The red blood cell (RBC) membrane is a composite structure, consisting of a fluid lipid bilayer and an underlying membrane-associated cytoskeleton. Both continuum and particle-based coarse-grained RBC models make use of a set of vertices connected by edges to represent the RBC membrane, which can be seen as a triangular surface mesh for the former and a spring network for the latter. We present a modeling approach combining an existing continuum vesicle model with a coarse-grained model for the cytoskeleton. The finitely extensible nonlinear elastic (FENE) spring force law in combination with a repulsive force defined as a power function (POW), called FENE-POW, is used to describe the elastic properties of the RBC membrane. The mechanical interaction between the lipid bilayer and the cytoskeleton is explicitly computed and incorporated into the vesicle model. We present three simulation examples to demonstrate the effectiveness of this hybrid continuum-coarse-grained model for the study of RBCs in fluid flows. This poster presentation is based on our recent paper (Lyu et al. 2018).

Introduction

The human red blood cells (RBCs) at rest are normally biconcave discocytes, and its membrane is composed of a lipid bilayer supported from inside by a two-dimensional (2D) triangular spectrin network of cytoskeletal proteins.

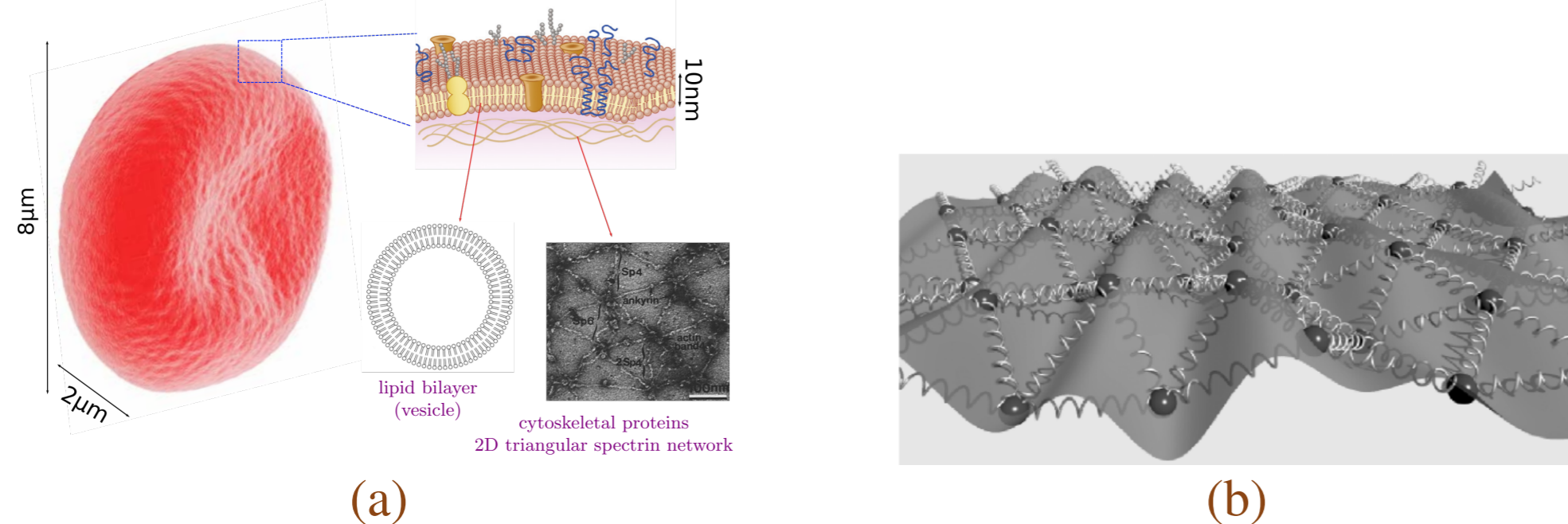


Figure 1: (a) A healthy human RBC and its membrane structure. (b) The cytoskeleton modeled as a spring network; the mechanical interaction between the spring network and the lipid bilayer at anchoring points (black beads). The aim of this work is to see if adding a spring network to a vesicle dynamics model (based on boundary element method in a Stokes flow) could be a possible way to build a RBC model.

The Model

– The lipid bilayer (position \mathbf{x} , velocity \mathbf{u}) as a vesicle dynamics model (Boedec et al. 2011)

$$\frac{d\mathbf{x}}{dt} = \mathbf{u}, \quad \text{div}_S(\mathbf{u}) = 0, \quad \mathbf{u} = \mathbf{P}\mathbf{G}\mathbf{f} + \mathbf{u}^\infty, \quad \mathbf{f} = \mathbf{f}^b + \mathbf{f}^\gamma + \mathbf{f}^e$$

\mathbf{G} the Green operator due to the Stokeslet, \mathbf{P} the projector onto a subspace of surface divergence-free vectors to satisfy the incompressibility constraint on the lipid's flow, \mathbf{f}^b the bending force, \mathbf{f}^γ the surface-tension-like force resulting from the Lagrange multiplier of the surface divergence-free constraint, \mathbf{f}^e the elastic force exerted by the spring network.

– The cytoskeleton (position \mathbf{y} , velocity \mathbf{v}) and its interaction with the bilayer (Lyu et al. 2018)

$$\frac{d\mathbf{y}}{dt} = \mathbf{v}, \quad \mathbf{v} \cdot \mathbf{n} = \mathbf{u} \cdot \mathbf{n}, \quad \Pi_{\text{tg}} [C_f(\mathbf{v} - \mathbf{u}) + \mathbf{f}^e] = 0$$

The operator $\Pi_{\text{tg}} = Id - \Pi_n$ the projector onto the tangent plan of the membrane surface, with $\Pi_n = \mathbf{n} \otimes \mathbf{n}$ the projector in the normal direction given by the normal vector \mathbf{n} pointing toward the outside bulk fluid, C_f the friction coefficient.

– The cytoskeleton elasticity – the FENE-POW spring model (Fedosov et al. 2010)

$$\mathbf{f}_n^e = \sum_p \frac{4\mu_S}{\sqrt{3} \left(\frac{2y_0^2}{1-y_0^2} + \alpha + 1 \right)} \left(\frac{1-y_0^2}{1-y_{np}^2} - \frac{y_0^{\alpha+1}}{y_{np}^{\alpha+1}} \right) (\mathbf{y}_p - \mathbf{y}_n),$$

We set $\alpha = 2$ and the ratio $y_0 = 1/2.05$. For a given shear modulus μ_S , and on the basis of the triangulation of cell membrane ($y_{np} = l_{np}y_0/l_0 = l_{np}y_0/l_{np}^0$) and its stress-free mesh ($l_0 = l_{np}^0$), the elastic force \mathbf{f}_n^e at node n by the edge np exerted by the spring network on the lipid bilayer can be obtained. The length of the link connecting vertices n and p is defined as $l_{np} = |\mathbf{y}_n - \mathbf{y}_p|$.

Numerical Examples

A Sedimentation

The first simulation example deals with a settling vesicle in combination with an underlying discrete spring network in an unbounded flow. Our objective here is to evaluate how effectively a cytoskeleton can influence the final shape of a settling vesicle.

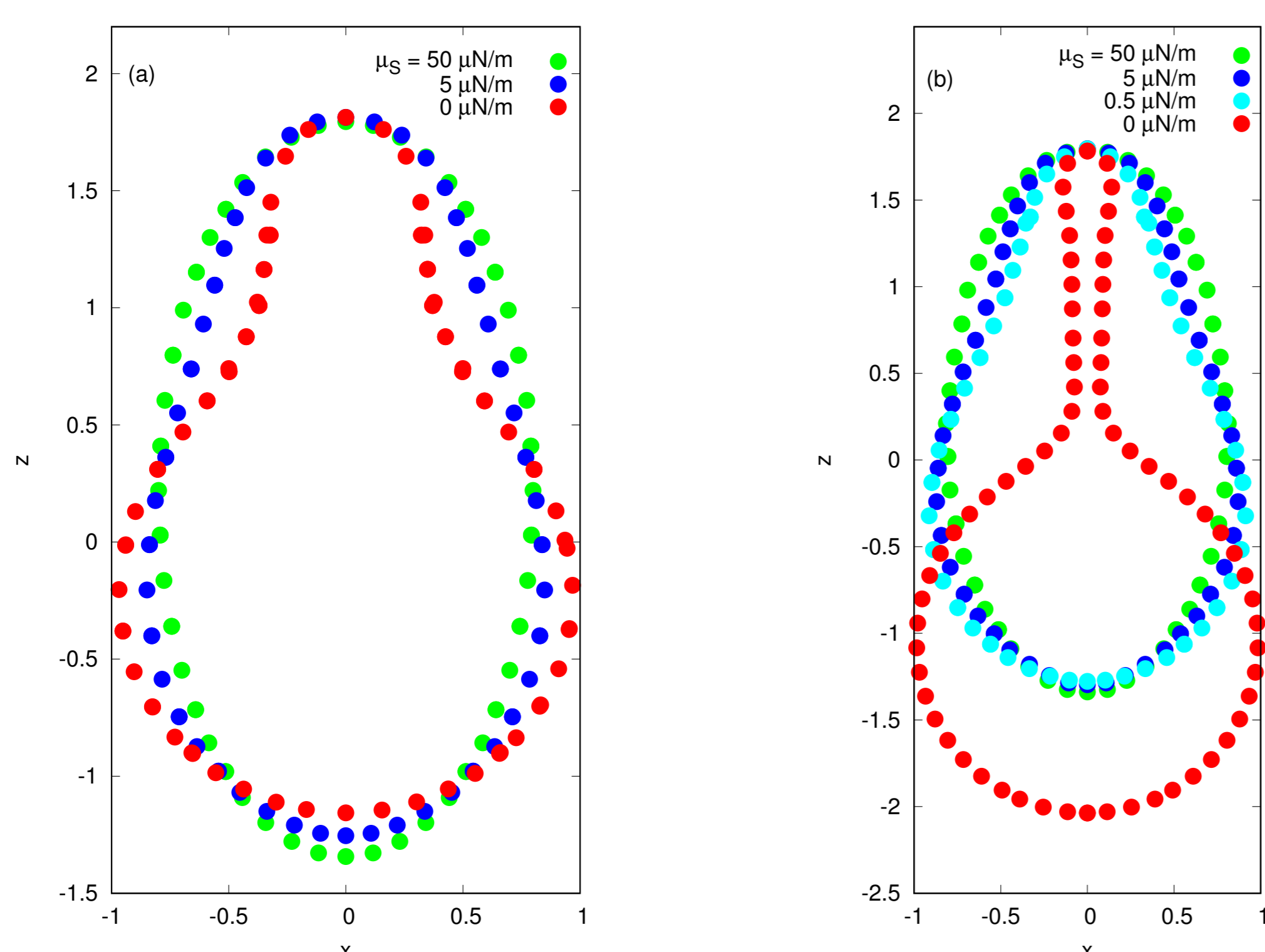


Figure 2: Stationary shape profiles of a vesicle-cytoskeleton model with reduced volume $\nu = 0.9$ for several values of μ_S and of the Bond number in the sedimentation simulations. (a) $Bo = 40$, (b) $Bo = 220$. In the case of a vesicle ($\mu_S = 0$ uN/m), there is a finger-like shape that disappears if we increase the value of the shear modulus μ_S . For high values of the shear modulus ($\mu_S > 50$ uN/m), the final shape is close to the initial reference one – a prolate ellipsoid. Coordinates are normalized with the equivalent radius of the vesicle R_0 . From this numerical experience, it is concluded that the emergence of long finger-like shapes can be observed only for vesicle sedimentation, since in the case of RBCs, even for large values of Bo , the cytoskeleton prevents the finger from appearing, indicating a significant interplay between vesicle dynamics and the cytoskeleton.

B RBC stretching

As a second numerical example, we perform RBC stretching simulations and compare our numerical results with the experimental data of RBC deformations by optical tweezers (Suresh et al. 2005).

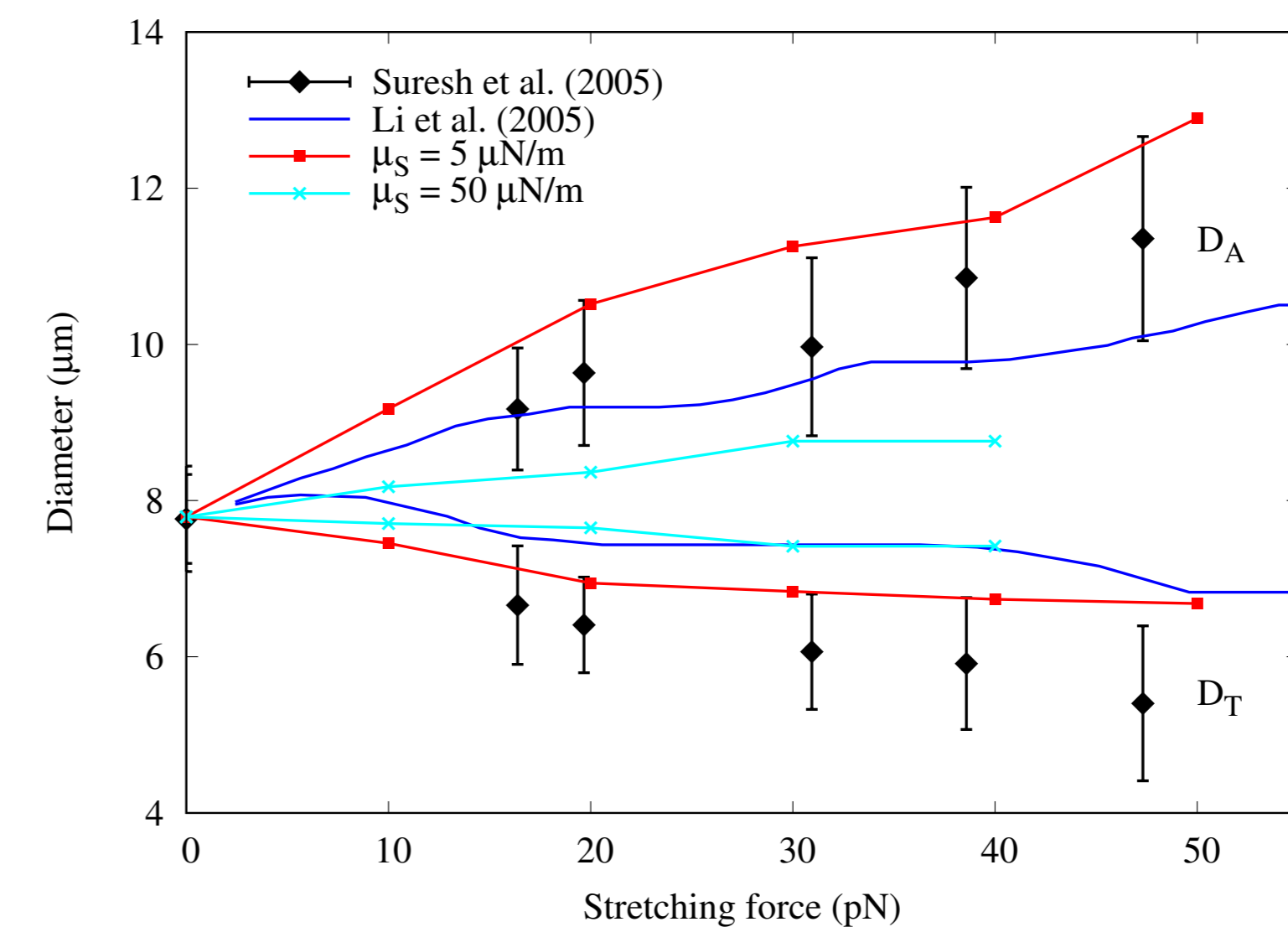


Figure 3: Variation of the axial D_A and transverse D_T diameter (μm) of RBC membrane as a function of stretching forces (pN) for two values of the shear modulus, $\mu_S = 5$ uN/m and $\mu_S = 50$ uN/m. Simulation results are compared with the optical-tweezers experiment (Suresh et al. 2005) and numerical predictions by a spectrin-level modeling (Li et al. 2005). As could be expected, the deformations of the RBC membrane in response to the applied stretching forces depend largely on the value of the shear modulus used in a numerical model.

C Motion of a single RBC in a capillary

The third simulation example concerns a single RBC in capillary flows. For practical issues, the transport of RBCs inside a capillary is a more relevant situation to consider. Two specificities of this class of flows contribute to RBC deformation: curvature of the Poiseuille type flow profile and confinement.

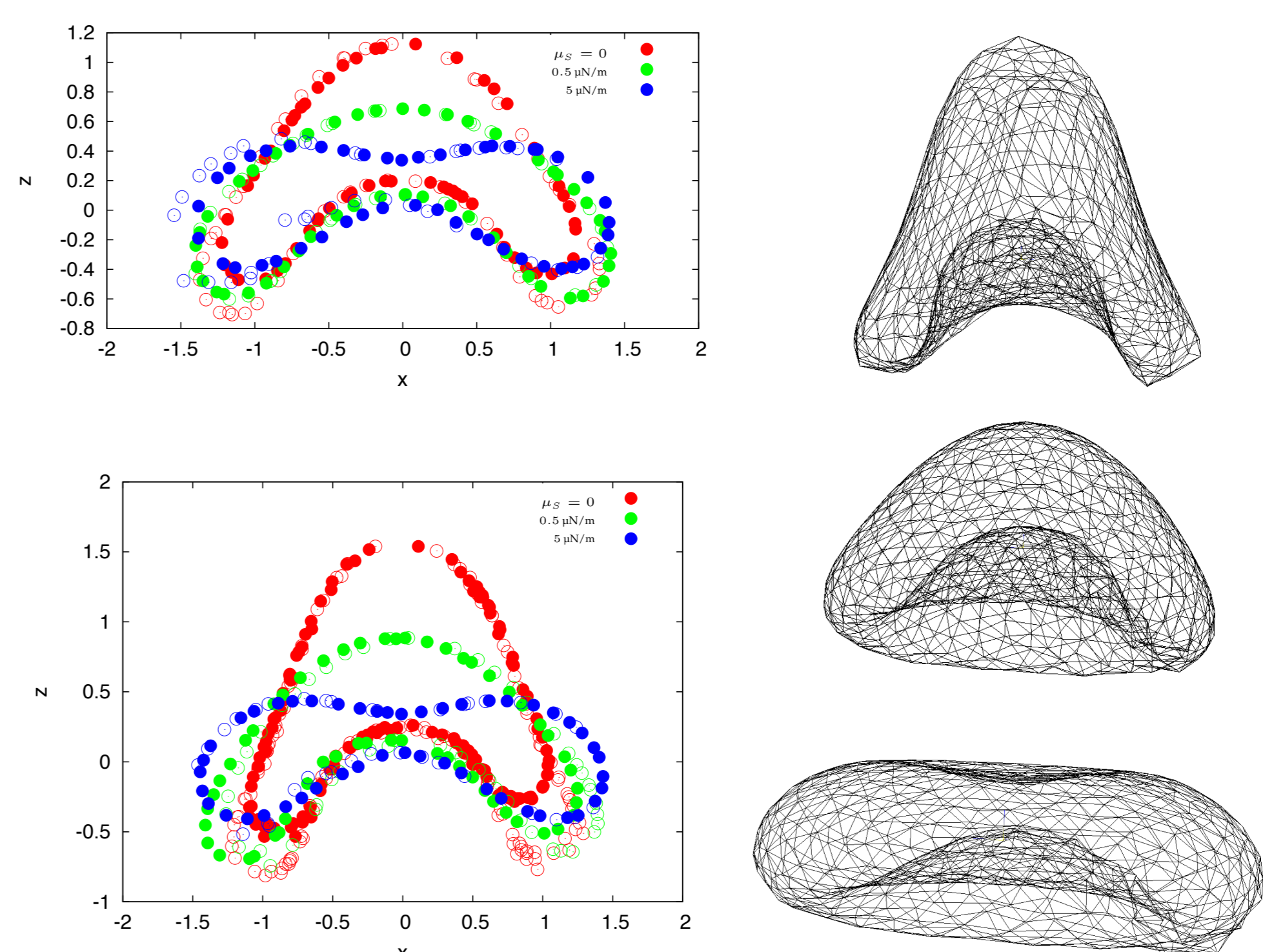


Figure 4: Stationary shape profiles obtained with the two-component vesicle-cytoskeleton model for a RBC transported in a capillary for increasing contribution of cytoskeleton, $Ca = 10$ and two confinement parameters: $\beta = 0.33$ (top left) and $\beta = 0.5$ (bottom left). Filled and unfilled circles represent the cross sections on the xz and yz plane, respectively. Coordinates are normalized with the equivalent radius of the RBC. The finite-element meshes, i.e. the state of the cytoskeleton corresponding to the shape profiles for $\beta = 0.5$ are shown on the right. A vesicle (red profiles) takes a typical parachute-like shape whose curvature increases with confinement and which can deviate from the axial symmetry. When the effect of a cytoskeleton is considered, even for a very weak shear modulus ($\mu_S = 0.5$ uN/m), large deformations of the parachute shape are reduced substantially, and the asymmetry of the cell becomes less significant. As the cytoskeleton strength is further increased ($\mu_S = 5$ uN/m) the cell recovers the discocyte shape typical of RBCs at rest. That means that hydrodynamic forces are not strong enough to oppose to cytoskeletal forces in order to allow shape deformation, and that the biconcave shape is more resistant to the flow stress.

Conclusions

- A hybrid RBC model, based on a combination of a spring network with a vesicle dynamics model, is proposed for the prediction of RBCs dynamics in a flow.
- The FENE-POW spring law is used for modeling the shear resistance of the cytoskeleton.
- The mechanical interaction between the bilayer and the cytoskeleton is explicitly computed.
- The model includes the fundamental mechanical properties of the RBC membrane: fluidity and bending rigidity of the lipid bilayer, and shear elasticity of the cytoskeleton while maintaining surface-area and volume conservation constraint.
- This work fills the gap between continuum mechanical modeling and coarse-grained modeling of RBC membranes by fusing these two approaches.
- There is a need for further development regarding the limitations that the test cases evidenced (stability issues, kinks).

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