

## Supplementary Information

We conducted a RBC mesh sensitivity study with cell mesh resolutions of  $N_V = 356$  and 2854 nodes to investigate quasi-static stretching and creep/relaxation dynamics. The cell deformation captured during stretching simulations are highly consistent in both cell models, but we do observe a slight dependence of mesh resolution on recovery. The relaxation responses are fit using the exponential

function,  $EI(t) = e^{-\left(\frac{t}{t_r}\right)^{\delta_r}}$  to calculate the time constants. The time constants for relaxation from a load  $f = 7\text{pN}$  are ( $t_r = 0.114 \pm 0.016$  s,  $\delta_r = 0.607 \pm 0.073$ ) for the cell model with 2854 nodes and ( $t_r = 0.084 \pm 0.013$  s,  $\delta_r = 0.604 \pm 0.013$ ) for 356 node model.

The triangulated cell models are closed manifold triangle meshes with Euler characteristic  $\chi = 2$  for each edge adjacent to at most two faces and each vertex having a disk-shaped neighbourhood. Hence, according to Euler-Poincare identity for polyhedral surfaces,

$$\text{Vertices } (N_V) - \text{Edges } (E) + \text{Faces } (F) = \text{Euler characteristic } (\chi) = 2$$

Since each triangle has 3 edges, and each edge belongs to 2 triangles,  $2E = 3F$ . Therefore,  $F = 2(N_V - 2)$  and  $E = 3(N_V - 2)$ .

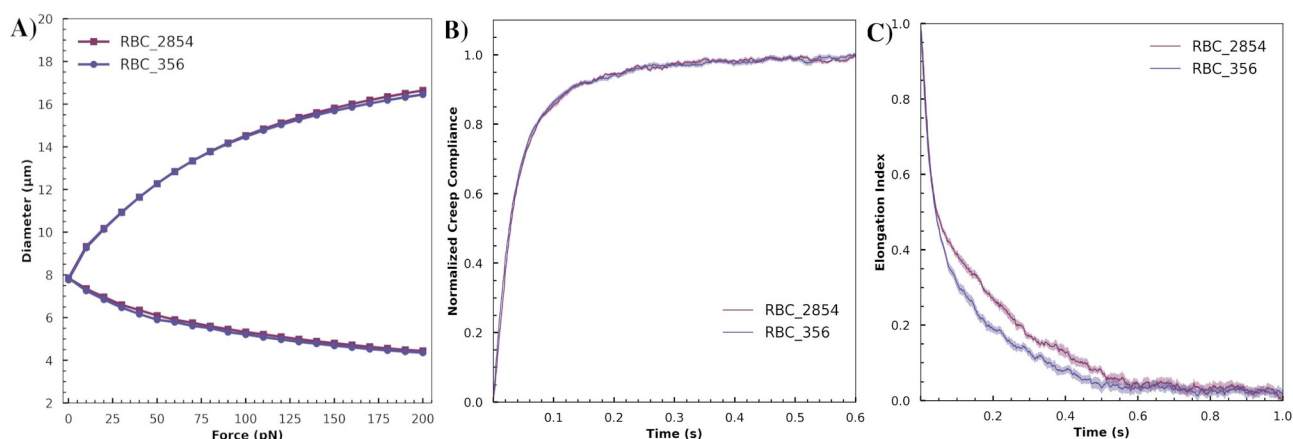


Fig. S1 Comparison of cell dynamics at mesh resolutions 356, and 2854 nodes subjected to A) quasistatic stretching, B) creep test, and C) relaxation test.

As the mesh resolution increases, the computational cost involving DPD interactions between fluid particles ( $N_F$ ) and the cell (represented by mesh nodes,  $N_V$ ), coarse-grained spectrin bonds (represented by mesh edges), local mesh area and volume (represented by triangles and tetrahedrons) increases substantially. A decent estimate of the computational cost as the mesh

resolution increases is given by,  $C \propto \left[ \left( \frac{(N_V + N_F) \ln(N_V + N_F)}{N_V \ln(N_V)} \right) + 3N_V + 2N_V + 3N_V \right]$

For the case of  $N_V = 2854$ , the computational time increases by approximately 65 times compared to the cell model of  $N_V = 356$ . Due to the above reasons, we believe that the current mesh model is a good choice with reduced computational cost and is effective in predicting cell dynamics.