Supplementary Materials: Simulation Methodology

Three-dimensional simulations using a front-tracking method are considered [1-3]. RBCs are modeled as liquid-filled elastic capsules of biconcave resting shape. The capsule is represented as a liquid drop surrounded by a zero-thickness elastic membrane. The interior and suspending fluids are assumed to be incompressible and Newtonian. The RBC membrane is assumed to possess a resistance against shear deformation, area dilatation, and bending. The resistance against shear deformation and area dilatation is modeled using a strain energy function developed by Skalak et al [4]

$$W = \frac{B'}{4}\left(\frac{1}{2}I_1^2 + I_1 - I_2\right) + \frac{C'}{8}I_2^2, \tag{1}$$

where B' and C' are physical constants, $I_1 = \epsilon_1^2 + \epsilon_2^2 - 2$ and $I_2 = \epsilon_1^2\epsilon_2^2 - 1$ are the strain invariants of the Green strain tensor, and ϵ_1 and ϵ_2 are the principal stretch ratios. Following Barthès-Biesel et al [5], (1) can alternatively be written as

$$W = \frac{G_s}{4}\left[\left(I_1^2 + 2I_1 - 2I_2\right) + C_S I_2^2\right], \tag{2}$$

where $G_s = B'/2$ is the surface shear elastic modulus, and $C_S = C'/2G_s$ is a constant that can be related to the membrane area dilatation. The area dilatation can be restricted by choosing a large value of C_S. The principal elastic stresses (or tensions) can be derived by the following equations

$$\tau_1^e \equiv \frac{1}{\epsilon_2}\frac{\partial W}{\partial \epsilon_1}; \quad \tau_2^e \equiv \frac{1}{\epsilon_1}\frac{\partial W}{\partial \epsilon_2}. \tag{3}$$

The RBC surface is discretized using flat triangular elements. A finite-element method is used to find the deformation gradient tensor $\mathbf{F}$, stretch ratios ϵ_1 and ϵ_2, and hence, the stress tensor $\boldsymbol{\tau}$ for each triangular element with linear shape functions [6,7]. Then, we use the principle of virtual work to estimate the elastic force in the membrane for each element as

$$\mathbf{f}_e = \sum_m \int_{S_m} \frac{\partial \mathbf{N}}{\partial \mathbf{X}} \cdot \mathbf{P} \, dS_0, \tag{4}$$

where $\mathbf{f}_e$ is the global nodal vector of external force acting on the fluid, $\mathbf{N}$ is the vector of linear shape functions commonly used for a triangular element, $\mathbf{P}$ is the first Piola–Kirchhoff stress tensor, and dS_0 is the element surface area in the unstressed original configuration. The stress tensor $\boldsymbol{\tau}$ is transformed to $\mathbf{P}$ using

$$\mathbf{P}^T = \epsilon_1\epsilon_2\,\mathbf{F}^{-1}\cdot\boldsymbol{\tau}. \tag{5}$$

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The bending resistance is modeled following Helfrich's formulation for bending energy [8]

$$W_b = \frac{E_b}{2} \int_S (2\kappa - c_o)^2 \, \mathrm{d}S \tag{6}$$

where E_b is the bending modulus, κ is the mean curvature, c_o is the spontaneous curvature, and S is the capsule surface area. The bending force density acting on the fluid can be derived by applying the first variation on W_b as

$$\mathbf{f}_b = E_b \left[(2\kappa + c_o) \left(2\kappa^2 - 2\kappa_g - c_o\kappa \right) + 2\,\Delta_{LB}\,\kappa \right] \mathbf{n} \,, \tag{7}$$

where κ_g is the Gaussian curvature, $\Delta_{LB} = (\mathbf{I}_s \cdot \nabla) \cdot (\mathbf{I}_s \cdot \nabla)$ is the Laplace–Beltrami operator [9], $\mathbf{I}_s$ is the surface projection tensor, and $\mathbf{n}$ is the unit vector normal to the surface and pointing outward. The mean and Gaussian curvatures are first evaluated at each vertex using a quadratic surface fitted to that vertex and its first-ring neighbor vertices. Then, the Laplace–Beltrami operator on the triangulated surface is evaluated using the surface gradient approximation of the mean curvature on each triangle [3].

The fluid motion is governed by the continuity and Navier–Stokes equations with an added body-force term as

$$\nabla \cdot \mathbf{u} = 0 \,, \tag{8}$$

$$\rho \left[\frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} \right] = -\nabla p + \nabla \cdot \mu \left[\nabla \mathbf{u} + (\nabla \mathbf{u})^T \right] + \int_S (\mathbf{f}_e + \mathbf{f}_b)\, \delta(\mathbf{x} - \mathbf{x}')\, \mathrm{d}\mathbf{x}' \,, \tag{9}$$

where δ is the three-dimensional Dirac–Delta function [10], $\mathbf{x}'$ is a Lagrangian point on the capsule surface, and $\mathbf{x}$ is a location in the flow. The membrane is advected as $\mathrm{d}\mathbf{x}'/\mathrm{d}t = \mathbf{u}_m$, where the membrane velocity $\mathbf{u}_m$ is obtained by interpolating the local fluid velocity $\mathbf{u}$ using the δ-function. A smooth representation of the δ-function spanning over four Eulerian points is used. The Navier–Stokes equations are solved by a projection method (for details, see [2]). A combined second-order finite difference scheme and Fourier transform is used for the spatial discretization, and a second-order time-split scheme is used for the temporal discretization of the Navier–Stokes equations.

To simulate microparticle adhesion to wall, we couple the above cell deformation and fluid flow model with the adhesive dynamics model in which formation of bonds between receptor molecules on particle surface and ligand molecules on the wall is simulated using a stochastic Monte Carlo method [11,12]. The receptors and ligands are randomly distributed

on surfaces. The probability of formation of a new bond, and that of breakage of an existing bond, in a time interval Δt, are given by

$$P_f = 1 - \exp(-k_f \Delta t),$$ (10)

$$P_r = 1 - \exp(-k_r \Delta t)$$ (11)

respectively, where k_f and k_r are the forward and reverse reaction rates which are computed as [12-14]

$$k_f = k_f^0 \exp\left(k_0 |l - \lambda| \frac{\gamma_c - 0.5|l - \lambda|}{k_B T} \right),$$ (12)

$$k_r = k_r^0 \exp\left(\frac{\gamma_c k_0 |l - \lambda|}{k_B T} \right),$$ (13)

where $\lambda = 150\text{nm}$ is the equilibrium bond length, $k_0 = 10$ nN/nm is the spring constant of bond, $\gamma_c = 1\ A^0$ is the reactive compliance, $k_f^0 = 500$ s^{-1} and $k_r^0 = 10$ s^{-1} are the zero-force forward and reverse reaction rates, respectively, $T = 310$ K is the temperature, and k_B is the Boltzmann constant [15]. At a given time instance, two random numbers N_1 and N_2, between 0 and 1, are generated. A new bond is allowed to form if $P_f > N_1$, and an existing bond is allowed to break if $P_r > N_2$ [12]. Bonds are assumed to stretch as linear springs and the force [14] in each bond is then obtained as

$$f_b = k_0 (l - \lambda).$$ (14)

The adhesive force is added to the Navier-Stokes equation using the Dirac-delta function as noted above.

REFERENCES

1. A. Yazdani and P. Bagchi, *J. Fluid Mech.*, 2013, **718**, 569-595.

2. S. K. Doddi and P. Bagchi, *Intl J Multiphase Flow*, 2008, **34**, 966-986.

3. A. Yazdani and P. Bagchi, *Phys Rev E*, 2012, **85**, 056308-056326.

4. R. Skalak, A. Tozeren, P.R. Zarda and S. Chien, *Biophys J*, 1973, **13**, 245.

5. D. Barthes-Biesel, A. Diaz, and E. Dhenin, *J. Fluid Mech.*, 2002, **460**, 211-222.

6. S. Shrivastava, and J. Tang, *J. Strain Anal.* 1993, **28**, 31-51.

7. C.D. Eggleton, and A.S. Popel, *Phys. Fluids*, 1998, **10**, 1834-1845.

8. W. Helfrich, *Z Naturforsch*, 1973, **C 28**, 693-703.

9. O.-Y. Zhong-Can, and W. Helfrich, *Phys. Rev. A*, 1989, **39**, 52805288.

10. G. Tryggvason, B. Bunner, A. Esmaeeli, N. Al Rawahi, W. Tauber, J. Han, S. Nas and Y. Jan, *J Comput Phys*, 20 01, **169**, 708-759.

11. G. I. Bell, M. Dembo, and P. Bongrand, it Biophys J, 1984, **45**, 1051-1064.

12. D.A. Hammer, and S.M. Apte, it Biophys J, 1992, **63**, 35-57.

13. M. R. King, and D. A. Hammer, *Biophys J*, 2001, **81**, 799-813.

14. M. Dembo, it Amer Math Soc, 1994, **26**, 51-77.

15. K. Chang, D. F. J. Tees and D. A. Hammer, *PNAS*, 2000, **97**, 11262-11267.