

A new theory for analyzing the time-dependent recovery of cells after large deformation

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Introduction

The ability of leukocytes (white blood cells) to undergo large deformation and then recover to their initial spherical shape has been exploited to determine the material properties of the cell. Leukocytes are nearly spherical with a diameter of about $8\mu\text{m}$ and their surface is covered by microvilli that protrude from the surface (Figure 1) (Kamm 2002). Most of our knowledge about leukocyte rheology has come from micropipette aspiration studies as shown in Figure 2. Rheological parameters for the cell are obtained by fitting the measured relaxation history to that of a theoretical model with an assumed constitutive equation for the interface. The most simple and common model considers the cell as a Newtonian droplet with constant surface tension interface. Nevertheless, it has been observed that the rheological properties of the cell are dependent on the deformation extent and rate, and that there exists a characteristic elastic response with a fading elastic memory (Marella and Udaykumar 2004). Based on this observation, we develop a model of a cell with an elastic membrane and compare its behavior to that of a clean drop.

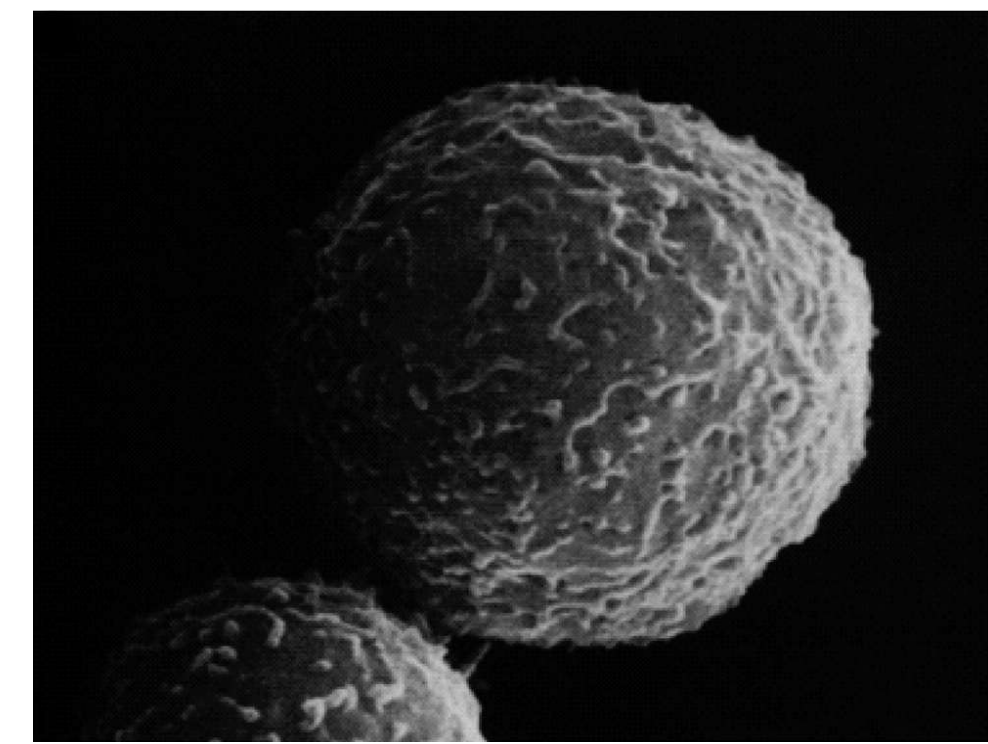


Figure 1. Scanning electron micrograph of neutrophils showing their spherical shape with numerous microvilli distributed over the surface. Reproduced from Dong and Skalak 1992.

- The specific objective of this work is to determine how the relaxation history of clean drops differ from that of a model cell with an elastic membrane enclosing a Newtonian fluid.

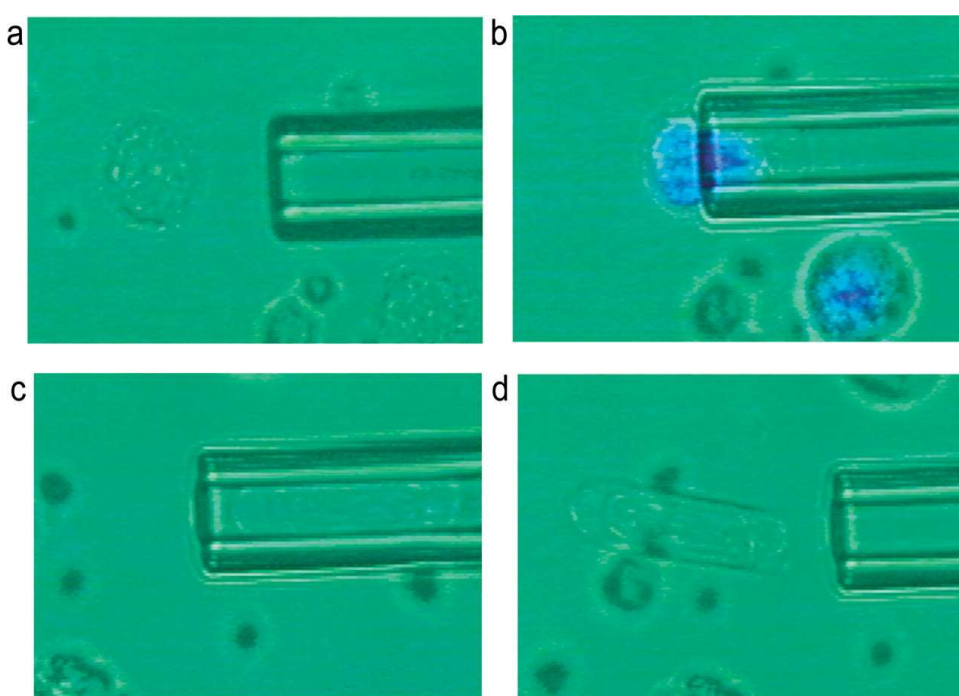


Figure 2. Micrographs showing the aspiration of a neutrophil into a micropipette. First the cell is drawn to the entrance of the pipette (a), by applying a pressure gradient the cell progressively flows in (b, c). When the pressure gradient is reversed, the cell can be ejected (d), and it eventually recovers its initial spherical configuration. Reproduced from Kamm 2002.

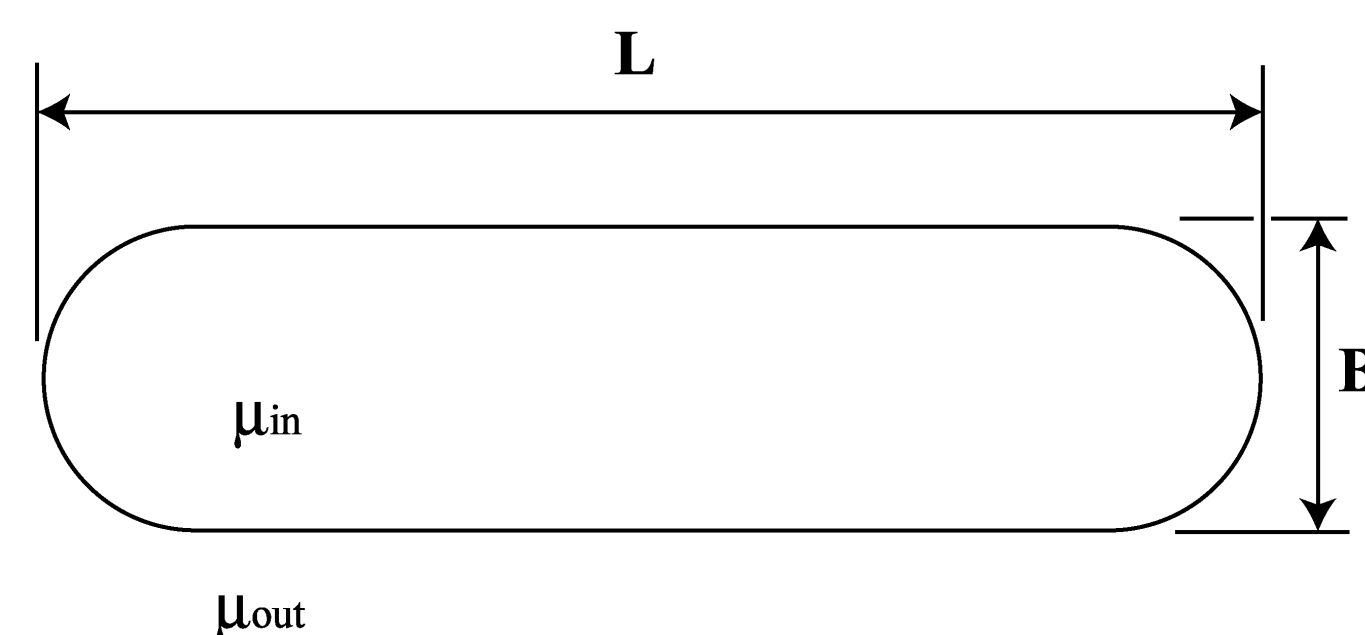


Figure 3. Schematic of the problem geometry showing the length, L , and the width, B of the capsule. The internal and external viscosities, μ_{in} and μ_{out} , respectively are also shown.

Methods

The complete axisymmetric Stokes equation coupled with the interfacial dynamic equations are solved using the boundary integral method. Two interfacial constitutive models are used, a clean drop with a constant surface tension, γ_e and a capsule with an elastic membrane which is modeled as a Hookean material. An initially deformed cell is allowed to relax in an otherwise quiescent fluid. The initial shape is that of a cylinder with a hemispherical cap on each side resembling the shape of a leukocyte after deformation in a micropipette (see Figures 2 and 3). The position of the membrane is recorded at regular time intervals. Non-dimensional parameters are defined to better characterize the relaxation of the cells, Table 1 lists these parameters. The instantaneous relaxation time, t_d^* (see Table 1 eq. 3), is calculated assuming that at each time the deformation parameter DF (see Table 1 eq. 1) follows the small deformation approximation (Velankar et al. 2004),

$$DF = D_0 \exp\left(-\frac{t}{t_d}\right)$$

Note that the instantaneous relaxation time, t_d^* , is not a measurement of the actual time it takes the cell to return to its original shape but it's a parameter related to the instantaneous slope of the relaxation curve.

$$DF = \frac{L-B}{L+B}; \quad \text{Where } L \text{ and } B \text{ are the principal lengths of the capsule (Fig. 3).} \quad (1)$$

$$\lambda = \frac{\mu_{out}}{\mu_{in}} \quad (2)$$

$$t_{drop}^* = \frac{t \gamma_e}{R_0 \mu_{in}}; \quad t_{Hookean}^* = \frac{t E_{sh}}{R_0 \mu_{in}} \quad (3)$$

$$t_{d,drop}^* = \frac{t_d \gamma_e}{R_0 \mu_{in}}; \quad t_{d,Hookean}^* = \frac{t_d E_{sh}}{R_0 \mu_{in}} \quad (4)$$

Table 1. Nondimensional parameters used for analyzing the relaxation of a capsule in an otherwise quiescent fluid. (1) DF is the Taylor relaxation parameter, (2) λ is the viscosity ratio, (3) t^* is the non-dimensional time with γ_e being the surface tension coefficient, E_{sh} the shear modulus for the Hookean membrane, R_0 the radius of a sphere with equal volume and (4) t_d^* is the non-dimensional relaxation time (see Velankar et al. 2004).

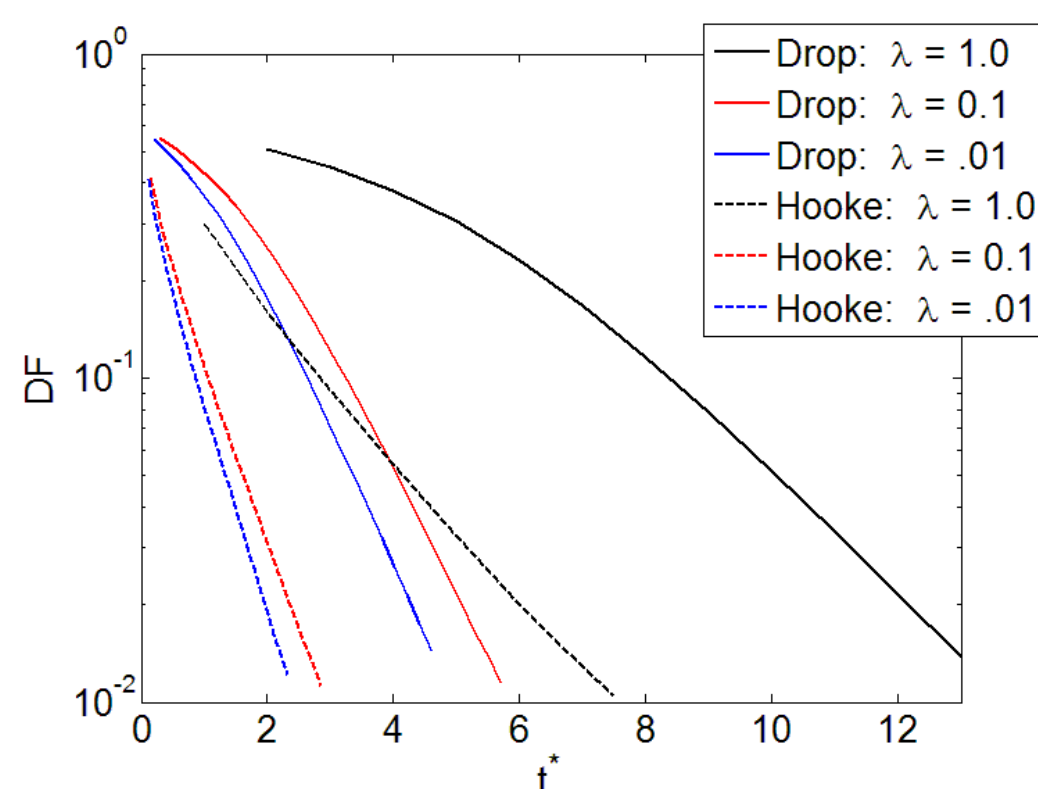


Figure 4. Deformation parameter, DF , as a function of non-dimensional time, t^* . Rate of relaxation is a function of viscosity ratio, λ , and membrane constitutive model.

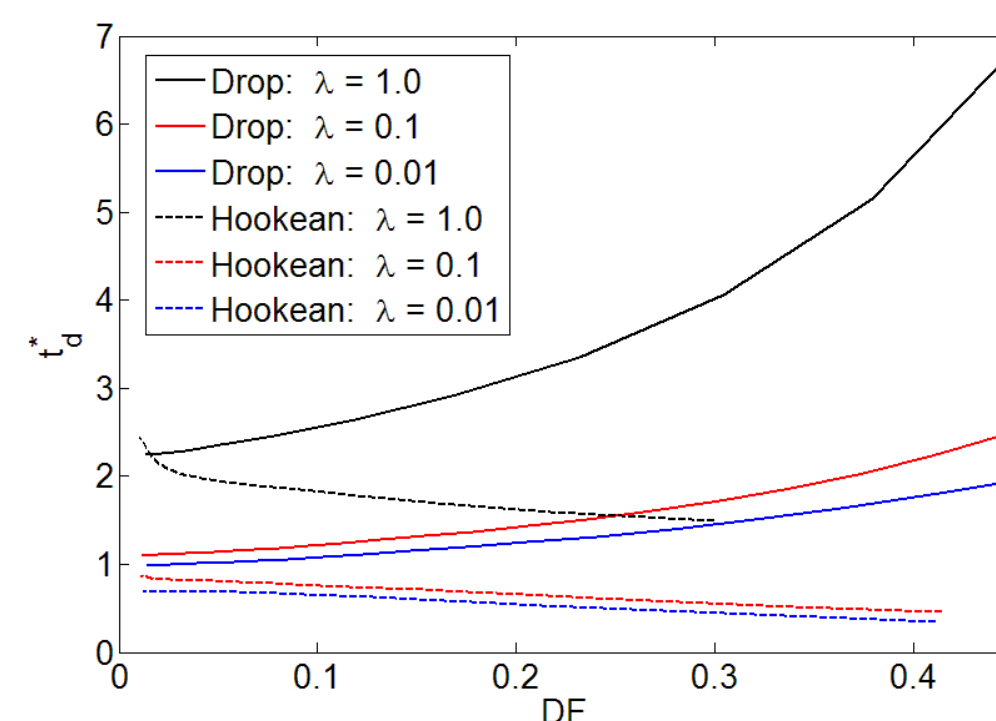


Figure 5. Non-dimensional instantaneous relaxation time, t_d^* , as a function of deformation parameter, DF .

Results and Discussion

Figure 4 shows that the evolution of the deformation parameter, DF , is dependent on the viscosity ratio, λ (see Table 1 eq. 2), and on the type of interfacial constitutive equation. Clean drops and elastic cell models both relax more slowly with increasing viscosity ratios. Also, the elastic membrane cell models relax faster than the clean drops at the same viscosity ratio and equivalent interfacial modulus, $\gamma_e = E_{sh}$. The instantaneous relaxation time (Figure 5) shows distinct differences between the behavior of clean drops and elastic membrane cells. For clean drops, the instantaneous relaxation time continuously decreases with decreasing deformation it continuously increases for the elastic cell models.

Conclusion

• Clean drops and elastic membrane cell models behave differently when relaxing in an otherwise quiescent fluid. The evolution of the deformation parameter, DF , but especially of the instantaneous relaxation time present characteristics unique to each interface which can aid in the development of better models when used in conjunction to analyze experimental data of actual cells.

References

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