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Mechanical Properties of Living Adherent Cells: Interaction of Cell and Shear flow

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Abstract. To investigate the interaction of the adherent cell and shear flow, a compound drop model was developed to simulate a living adherent cell adhered to a smooth substrate, and a two dimensional computational fluid dynamics (CFD) was conducted to solve the model equations. The results showed that the deformability of the cell increases with Reynolds number and initial contact angle. The nucleus deforms with the cell, and the deformation index of the cell is greater than that of the nucleus. The cell is more deformable while the nucleus is more capable of resisting external shear flow. The cell and the nucleus are not able to deform infinitely with the increase of Reynolds number and the deformation index reaches a maximum. We conclude that the nucleus plays a particular role in the mechanical properties of the adherent cell.

Introduction

Cell adhesion on scaffold or matrix is a key process in which the balance between hemodynamic and adhesion forces (molecular bonds) plays an important role [1]. According to hemodynamic theories, shear flow induces the change of the shape and the spatial arrangement of the adhered cell. These changes may in turn develop the redistribution of shear stress around the cell. Therefore there exists interaction between the adherent cell and shear flow. It is critical to understand how shear flow induces the changes of mechanical properties of the adherent cell.

Studies using parallel flow chamber and radial flow assays show that the stiffness of cell increases when cells are allowed to spread or after adaption to flow, both conditions being associated with a remodeling of the cytoskeleton [2]. However, most of these models are based on the hypothesis that the cell is a solid sphere. More recently, a single drop model considering the cell as a viscous liquid drop was developed to simulate the adherent cell behavior [3], but the presence of the nucleus was neglected. However, it is known that the mechanical properties of the nucleus may play a major role in mechano-transduction [4,5]. Therefore, a compound cell model, which accounts for the role of nucleus, is more appropriate for modeling the mechanical properties of the cells.

The objective of this work is to study the deformation of the adherent cell and confirm if the nucleus deforms with the cell. Our attention is paid particularly to the importance of Reynolds number of the imposed shear flow, and the initial contact angle on the deformation of the model cell.

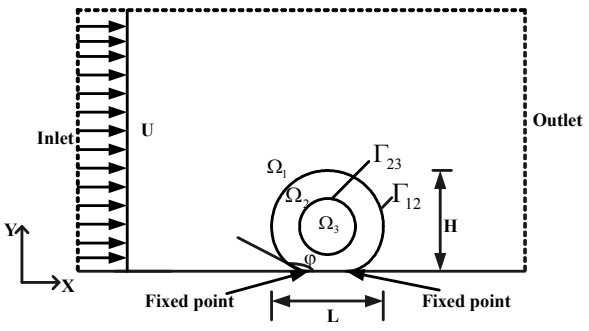

Fig.1 Illustration of the simulated model cell and the parameters in the analysis

Material and Methods

Modeling and governing equations. We simplify the adherent cell (model cell) to two fluid components: one is the nucleus and one is the rest of the cell, here after called cytoplasm. The physical situation of the compound drop corresponds to three incompressible fluids with the density of ρ_i and viscosity μ_i, which occupy the region Ω_i (i=1,2,3). The regionsΩ_1, Ω_2, Ω_3 represent, respectively, the flowing fluid, cytoplasm, and nucleus (Fig.1). Surface tensions σ_{12} and σ_{23} at the interfaces of Γ_{12} and Γ_{23} are assumed to be constant. R_c and R_n are the initial radii of the cell and the nucleus respectively.

The choice of characteristic length, time, and pressure are as follows:

$$L = R_c, \qquad T = \frac{1}{G}, \qquad P = \frac{\mu_1 U}{L}. \tag{1}$$

where G is the nominal shear rate calculated from Poiseuille's equation of an established flow, U is the mean velocity of exposed flow. According to Navier-Stokes equations at low Reynolds number, the dimensionless governing equations for a compound drop can be formulated by equations (2) to (5):

$$\nabla \cdot V_i = 0. \tag{2}$$

$$0 = -\nabla p_1 + \lambda_1 \nabla^2 V_1 + \frac{\gamma_c}{N}\int n_2 \delta(x - x_m) d\Gamma_{12}. \tag{3}$$

$$0 = -\nabla p_2 + \lambda_2 \nabla^2 V_2 + \frac{\gamma_c}{N}\int n_2 \delta(x - x_m) d\Gamma_{12} + \frac{\gamma_n}{N}\int n_3 \delta(x - x_m) d\Gamma_{23}. \tag{4}$$

$$0 = -\nabla p_3 + \lambda_3 \nabla^2 V_3 + \frac{\gamma_n}{N}\int n_3 \delta(x - x_m) d\Gamma_{23} \quad . \tag{5}$$

where $\lambda_i = \frac{\mu_i}{\mu_1}$, $(i = 1,2,3)$, represents the nondimensonal viscosity of imposed fluid, cytoplasm, and nucleus respectively. V_i and p_i represent the velocity vector and pressure in region Ω_i, respectively. n_i is the unit normal vector, defined as positive when pointing outward from each region i; $x_i = \nabla \cdot n_i$ is the local mean curvature of the interface; x and x_m are the locations of points in the flow field and on the interface, respectively, δ denotes the delta function, varying with initial contact angle φ. $\gamma_c = 1$ and $\gamma_n = \sigma_{23}/\sigma_{12}$ are the nondimensional surface tensions of the cytoplasm and nucleus, respectively. $N = \mu_1 G R_c / \sigma_{12}$ denotes a measure of the relative dominance of viscous forces to surface tensions. The integral terms in equations denote the Eulerian force contributions of the normal stress discontinuity due to capillary forces evaluated on the interfaces Γ_{ij}. These forces are transmitted from the interfaces to the fluid by use of the Immersed Boundary Technique [6].

Numerical Resolution. It was assumed that there is a uniform inlet velocity with an entrance length sufficient to have an established Poiseuille flow before flow reaches the disturbed flow region near the model cell. The boundary conditions to be satisfied on each interface for cases involving no mass exchange across it are the continuity condition and the stress balances.

The Reynolds number (Re) is defined as:

$$\mathrm{Re} = \frac{\rho_1 UD}{\mu_1}. \tag{6}$$

where D is the diameter of the vessel.

As an example, we consider the case of a leukocyte adhering to the wall of blood vessel. The value of R_n is dependent on R_c since the nucleus occupies a volume of 21 percent of the neutrophils, the most common leukocyte in circulation [7]. The model parameters are applied based on previous studies as listed in table 1.

Table 1 Parameter estimations in the model for leukocytes

Symbol	Value
ρ_1	1×10^{-3} [kg/m^3]
μ_1	1×10^{-3} [Pa•s]
λ_1	1
λ_2	100
λ_3	1000
γ_c	1

To examine the deformation of a cell adhered to the surface of vascular under shear flow, we introduce the deformation index (DI) as follows:

$$DI = (l/h)/(L_i/H_i) \tag{7}$$

where L_i and H_i are, respectively, the initial length and height of the cell; l and h are the length and height after deformation respectively. We will investigate the influences of the initial contact angle (φ), and the Reynolds number (Re) on the deformation index (DI).

A finite volume solution package (Fluent 5, Fluent Incorporated, USA) on a Sun Ultra 10 workstation is used to solve the Navier-Stokes equations for low Reynolds number (Re) flow in a cylindrical tube with one model cell adhered to the vessel wall. The calculations are performed in two dimensions, and the criterion for convergence is at least a five order of magnitude reduction in the total residuals.

Results

Effects of imposed shear flow on cell deformation. Fig. 2 shows the deformation of a compound drop changes with the applied shear flow at controlled conditions (N=0.01, φ=150°). As the applied flow strength increases, the cell experiences substantial stretching. At the same time, the nucleus does experience deformation with the cell.

Fig.3 summarizes the effects of Reynolds number (Re) on the deformation indices of the cell and the nucleus. It is shown that there is a low level of cell deformation if Re is smaller enough (<0.0005). If Re is between 0.0005 and 0.05, the deformation index increases greatly with Re until it reaches a summit which is maintained even if Re is greater than 0.05. We can also find that the cell is more likely to deform than the nucleus, while the nucleus is more capable of resisting external flow under controlled conditions.

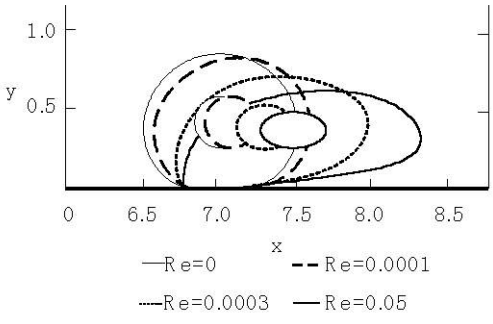

Fig.2 Effect of Reynolds number (Re) of the imposed flow on the deformation of the compound drop with N=0.01 and φ=150°.

Effects of initial contact angle on cell deformation. Fig.4 shows the changes of the deformation indices (DI) of the cell and the nucleus at different initial contact angles under identical conditions (N=0.05, Re=0.005). It clearly indicates that at a small initial contact angle, the deformation indices of the cell and the nucleus are increased with the increase of the initial contact angle. Then, the deformation indices are increased hardly at all when the initial contact angle increases. The

deformation index of the cell is always greater than that of the nucleus at an identical initial contact angle.

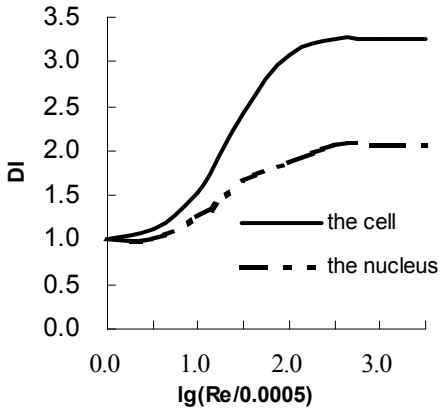

Fig.3 Dependence of the deformation indices (DI) on Reynolds number (Re) of the imposed flow with φ=150° for the cell and the nucleus.

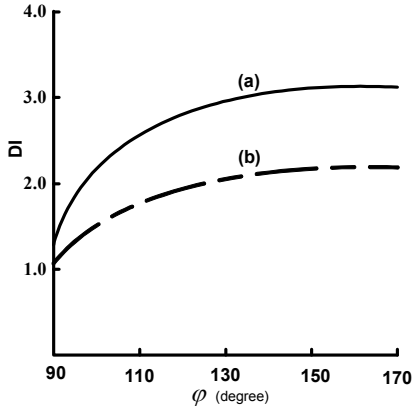

Fig.4 Dependence of the deformation indices (DI) on the initial contact angle (φ) for the cell and nucleus with N=0.05 and Re=0.005. (a) the cell; (b) the nucleus.

Conclusion and Discussion

This study is aimed at characterizing the deformation mechanism of a cell adhered to vascular surface under steady shear flow. A compound drop model is proposed to elucidate the dynamics of cell deformation in an idealized situation. By introducing the parameter of deformation index (DI), we found that both of the cell and the nucleus are capable of deformation. The cell becomes more elongated when either initial contact angle or Reynolds number increases.

As Reynolds number of the imposed flow increases, the cell tends to spread over the surface of the wall, increasing the area of contact and strength of the adhesion. Cell-substrate interaction is also manifested through the initial contact angle of the cell with the surface, which can determine how the cell will react to hydrodynamic forces. For instance, a cell having a higher initial contact angle with surface will spread more than having a smaller one. These findings are also important to issue on how cell react to biomaterials or artificial organ.

Acknowledgments

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