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Effect of Pseudopod Extensions on Neutrophil Hemodynamic Transport Near a Wall

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Abstract

During inflammation, circulating neutrophils roll on, and eventually tether to, the endothelial lining of blood vessels, allowing them to exit the bloodstream and enter the surrounding tissue to target pathogens. This process is mediated by the selectin family of adhesion proteins expressed by endothelial cells. Interestingly, only 10% of activated, migrating neutrophils transmigrate into the extravascular space; the other 90% detach from the wall and rejoin the blood flow. Neutrophils extrude pseudopods during the adhesion cascade; however, the transport behavior of this unique cell geometry has not been previously addressed. In this study, a three-dimensional computational model was applied to neutrophils with pseudopodial extensions to study the effect of cell shape on the hydrodynamic transport of neutrophils. The collision time, contact area, contact force, and collision frequency were analyzed as a function of pseudopod length. It was found that neutrophils experience more frequent collisions compared to prolate spheroids of equal volume and length. Longer pseudopods and lower shear rates increase the collision time integral contact area, a predictor of binding potential. Our results indicate that contact between the neutrophil and the vessel wall was found to be focused predominantly on the pseudopod tip.

Key Terms

Hydrodynamics; Computational modeling; Pseudopod; Neutrophil

INTRODUCTION

Inflammation is a key physiological process, important in infections, autoimmune diseases, and chronic diseases, including cancer, Alzheimer's, and heart disease. Accounting for half of circulating leukocytes, neutrophils are the body's principal defense during acute inflammation and act within minutes of a triggering event^{27,32}. In circulation, red blood cells drive neutrophils towards the endothelium, away from the center of the venule, allowing them to interact with the vessel wall^{8,26}. During an innate immune response, neutrophils in the circulation roll on, and eventually tether to, the endothelial lining of blood vessels, which

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CONFLICTS OF INTEREST

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ETHICAL STANDARDS

No human studies were carried out by the authors for this article. No animal studies were carried out by the authors for this article.

allows them to exit the bloodstream and enter the surrounding tissue to target invading pathogens.

In the postcapillary venules, the tethering and rolling of freely flowing neutrophils prior to extravasation is largely mediated by the selectin family of transmembrane glycoproteins, which includes P-selectin, E-selectin, and L-selectin^{21,25}. After endothelial cells are stimulated during an inflammatory event, P-selectin is expressed first, then E-selectin, both of which bind to P-selectin glycoprotein-1 (PSGL-1) on the surface of neutrophils to facilitate tethering and rolling. Adhesion and crawling are mediated by integrins, namely intercellular adhesion molecule 1 (ICAM-1) and vascular cell adhesion molecule 1 (VCAM-1)¹⁹.

The neutrophil rolling and adhesion paradigm for extravasation is not necessarily a one-way process. It has been shown *in vivo* that only 10% of activated, migrating neutrophils transmigrate into the extravascular space, while the vast majority detach from the wall and rejoin the blood flow³¹. During inflammation, neutrophils extrude pseudopods (also called lamellipods) that are essential in crawling on the endothelium and eventually extravasating into the extracellular space. Pseudopods are organelle-less extensions that grow and retract due to the polymerization of actin filaments; once extruded, they remain stiff^{7,11,33}. Four percent of leukocytes freshly-harvested from human whole blood exhibited pseudopod projections⁶. There is an interesting, yet unstudied, population of circulating neutrophils with pseudopods that are stable for the time scale displayed *in vivo*. In this study, we examined how this pseudopodial extensions affect blood vessel wall collision behavior using a three-dimensional hydrodynamic model.

Existing multiscale three-dimensional computational models to understand cell rolling comprise interconnected mechanical (hydrodynamic motion) and chemical (adhesion kinetics) components. The physics of near-wall sphere rotation was first analyzed by Jeffery in 1915¹². The first direct model of leukocyte rolling, called Adhesive Dynamics (AD), was developed by Hammer and Apte in 1992⁹. It was revised by King and Hammer in 2001 for multiple particles, termed Multiparticle Adhesive Dynamics, MAD^{15,16}. Near-wall rolling behavior involves bond formation and dissociation with the wall, and MAD couples the hydrodynamics and adhesion kinetics components. Other leukocyte rolling models have been semianalytic, analytical, or agent-based, but all of these consider the rolling adhesion of (at least initially) spherical neutrophils^{14,29}. MAD, based on the Completed Double Layer Boundary Integral Equation Method (CDL-BIEM), is used to solve the integral representation of the Stokes equation in simple shear flow. It has been adapted for rigid spherical leukocytes^{2,4,5,18} and oblate spheroids representing platelets in the bloodstream^{22–24,30}. MAD produces physiologically-relevant cell rolling and collision behavior while incorporating experimentally-determined bond formation and dissociation kinetics. The MAD algorithm uses Monte Carlo to determine individual bond formation/dissociation events at each time step based on bond kinetics (in this case, PSGL-1 and P-selectin). The bond force calculations yield the net force and torque acting on the cell, which are then fed into hydrodynamic equations to calculate 3-D mobility. Here, we have utilized the hydrodynamic component of MAD in the development of a model to examine the collision behavior between neutrophils with stiff pseudopodial extensions and the vessel

wall. Specifically, we analyzed how pseudopods affect collision time and contact area, contact force, and collision frequency, parameters that control binding potential. We focus on the rolling hydrodynamics in order to identify the physiological role of neutrophil pseudopodial extensions in the transmigration process.

METHODS

Hydrodynamic calculation

CDL-BIEM represents the creeping motion of a rigid cell in a three-dimensional area representing a fluid domain bounded by an infinite plane at $z = 0$ (Figure 1). For this study, a Gaussian-shaped extension was projected out of one side of the sphere to represent a neutrophil body with pseudopod, creating one axis of symmetry. The endothelial wall was modeled as a plane. The Reynolds number is calculated as $N_{RE} = \gamma \rho a^2 / \mu = O(10^{-2}) < 1$. The shear rate, $\gamma = 1000 \text{ s}^{-1}$ unless otherwise specified, is within the physiological range; ρ is the density of blood plasma $= 1.0239 \text{ g cm}^{-3}$; μ is the viscosity of blood plasma $\approx 1 \text{ cP}$; and a is the cell radius, here the hydrodynamic radius $4 \text{ }\mu\text{m}$ for all cell geometries. Thus, the linear shear flow with velocity gradient in the z -direction is within Stokes regime. The Stokes equation is:

$$\nabla p = \mu \nabla^2 u, \nabla \cdot u = 0 \quad (1)$$

Where p is the pressure, μ is the fluid viscosity, and u is the velocity. The ambient flow is approximated as linear shear flow:

$$u_{\infty} = \gamma z \quad (2)$$

Where γ is the shear rate, and z is the vertical distance from the center of mass of the particle to the flat wall. No slip conditions on all surfaces is assumed. At the surface of the wall, the velocity is zero:

$$u_{z=0} = 0 \quad (3)$$

The integral representation of the Stokes equation is:

$$u_j(X) + \int_S n_k(x) \sum_{ijk} (x, X) u_i(x) dS(x) = \int_S G_{ij}(x, X) \sigma_{ki}(x) n_k(x) dS(x) \quad (4)$$

where G_{ij} is the singularity solution due to a point force acting on the bounding surface S at x , acting in the j direction at point X in the fluid. n is the normal vector at x pointing outward into the fluid, σ is the stress tensor and is given by

$$\sigma = -pI + \mu [\nabla u + (\nabla u)^t] \quad (5)$$

where t indicates the transpose operator and I is the identity matrix. Σ_{ijk} is the ik th component of the stress tensor corresponding to flow produced by a point force at x in the j direction.

Short-range repulsive force calculation

Steric layers were added to the particle and wall (0.175 μm and 0.05 μm , respectively) to represent the roughness of the cell membrane and the glycocalyx molecules on the cell surface¹⁵. The short-range repulsive force representing the contact force between surfaces is:

$$F_{rep} = F_0 \frac{\tau e^{-\tau \varepsilon}}{1 - e^{-\tau \varepsilon}} \quad (6)$$

Where ε is the distance between the outer edges of both steric layers, F_0 was set at 1×10^{15} fN, and τ was set at 2000 μm^{15} . Although the cell is rigid, the force that the cell exerts on the wall in the y -direction can compress the glycocalyx³⁴.

Numerical calculation

The CDL-BIEM code is implemented in FORTRAN 95 (IBM Corporation, Armonk, NY) and double-precision was used for all calculations. The cell's surface was meshed initially as a cube with faces containing 4×4 Lagrangian (QUAD9) elements, a total of 96 elements. Each QUAD9 element contained nine nodes: one node in the center, nodes at each of the corners, and nodes at the center of each of the edges. This cube was superimposed onto the cell geometry with the center of cube coincident with the center of the spherical cell body. Maintaining the cell volume constant, the pseudopod lengths studied ranged from 1.1 to 1.9 times the spherical body radius (see Figure 2). The neutrophil shapes were compared to prolate spheroids of equivalent major axis length and volume (Figure 2). Prolate spheroids were chosen for comparison because their near-wall and unbounded convective transport have been studied previously^{13,20}. In contrast to the pseudopod-extending neutrophil shape, prolate spheroids have two axes of symmetry and at most one point of contact with the wall. Unless otherwise specified, the initial simulation condition was the cell oriented with its major axis parallel to the wall and the pseudopod oriented downstream in the direction of flow.

Hydrodynamic validation of the model

The calculated Jeffery orbits of spheroids were compared with the CDL-BIEM simulation for model validation. A spheroid is described to exhibit Jeffery orbits if there is no lateral motion in unbounded shear flow¹³. The spheroid's surface was meshed with 384 elements instead of 96 as with all other simulations for increased precision. The spheroid was placed at an initial centroid height of 40 μm away from the surface, sufficiently far for wall effects to be negligible. The orientation angle in the y -direction over time is shown for spheroids of length 1.9 and 1.1 in Supplementary Figure 1a and 1b, respectively. Time is non-dimensionalized with the reciprocal shear rate; the dimensionless centroid height and lowpoint values were normalized to the cell's hydrodynamic radius of 4 μm .

Parameters evaluated

A range of pseudopod lengths was systematically tested under physiologically-relevant shear flow rates. The effects of initial height and angle on each cell's trajectory and the effect of shear rate on the binding potential were studied. A collision event was recorded if any part of the cell came within a "reactive" distance of the endothelial surface; here, it was set at $0.26\text{ }\mu\text{m}$, the total length of a P-selectin/PSGL-1 bond, $0.08\text{ }\mu\text{m}$ ¹⁷, plus typical steric layers²⁸. Metrics quantified for each cell trajectory simulation included contact time, maximum contact area, and time integral contact area. Contact time was calculated as the total time that any part of the cell was within potential binding range of the wall. Maximum contact area was defined as the area of the cell surface that is within a reactive distance to the wall during one full rotation. Time integral contact area (TICA) was defined as the integrated product of contact time and contact area and is taken to be a predictor of binding potential. Another predictor of binding potential is the contact force exerted by the cell perpendicular to the wall (in the z -direction) during a collision event. Contact force at a time step was calculated as the acceleration of the cell in the z -direction (integral of the centroid's position at the current and previous time steps) multiplied by the mass of a typical leukocyte, $1.08 \times 10^{-12}\text{ g}$ (calculated from the mass density³⁴).

RESULTS

Neutrophils with pseudopods display irregular tumbling trajectories

Longer lengths caused neutrophils and prolate spheroids to undergo more lateral translation during tumbling. Figure 3 presents a "side view" of tumbling trajectories of an equivalent neutrophil and a spheroid of length 1.9 under the same conditions. Lowpoint and centroid height trajectories (Figure 4 and Figure 5, respectively) were analyzed for both neutrophils and spheroids at initial heights $R/2 - 3R$ away from the wall, where R is the hydrodynamic radius of $4\text{ }\mu\text{m}$. The lowpoint was defined as the minimum distance between the cell's surface and the endothelium, not including the surface roughnesses. A variety of initial lowpoints were examined to determine whether free-flowing neutrophils could collide downstream with the endothelium. At lower initial heights ($R/2$ and $R/4$), longer pseudopods propel the neutrophil away from the endothelial wall (Figure 4c). The neutrophil centroid height remained at a higher height thereafter in the absence of gravitational sedimentation (Figure 5c), called "pole vaulting." Similar behavior was seen for spheroids at an initial height of $R/4$ (Figure 4d and Figure 5d). When the initial starting height was higher and no collision occurred, the lowpoint and centroid trajectories for both neutrophils and prolate spheroids showed that the height was maintained over time (Figure 4a and b and Figure 5a and b). At the highest starting heights studied, prolate spheroid centroid heights remained steady over time, without bobbing; as the vessel wall had no effect on these trajectories, the particles exhibited classic Jeffery orbits (Figure 5c). At higher initial heights (above $R/2$ for neutrophils and $R/4$ for spheroids), period length remained consistent; this was due to the Jeffery orbit motion (Figure 4a and b and Figure 5a and b). When neutrophil and equivalent spheroid trajectories are compared, it is evident that neutrophils display higher centroid heights and lower lowpoints; i.e., they are observed to bob up and down more. Thus, remaining closer to the wall gives the neutrophil more binding potential.

Neutrophils experience more frequent collisions than prolate spheroids of equal volume and length

Next, wall collision frequency was examined for neutrophils and spheroids of varying lengths and at different initial heights. In Figure 6, diagonal lines show conditions under which particles made contact with the wall. Comparing the wall collision frequency of neutrophils and spheroids of varying length and initial height, neutrophils were found to experience more frequent collisions than spheroids of equivalent length. For example, neutrophils of length 1.3 collided with the wall at initial heights up to 1 μm , whereas spheroids of this length experienced collisions up to a height of 0.5 μm . The longest neutrophil length studied (1.9) collided with the wall up to an initial height of 2 μm , whereas the equivalent spheroid only experienced collisions up to an initial height of 1.5 μm . More frequent collisions provide more opportunities for bond formation, suggesting that neutrophils will have a greater probability than spheroid geometries of tethering with the wall.

Longer pseudopods and lower shear rates increase TICA during collisions

The collision TICA was studied for a range of neutrophil and spheroid lengths and initial heights, as it is an indication of binding potential. In Figure 7, the TICA are shown for neutrophils (a) and spheroids (b). The length aspect ratios studied were 1.1, 1.3, 1.5, 1.7, and 1.9, and the initial heights ranged from 0.5–3 μm . For both neutrophils and spheroids, contact time usually increased for longer lengths and decreased as the initial height was increased (Supplementary Figure 2a and c). Similar trends were observed for maximum contact area for both geometries (Supplementary Figure 2b and d). The TICA graphs showed a similar pattern (Figure 7a and b). Spheroids showed greater contact times, greater maximum contact areas, and TICA than neutrophils at lower initial heights, yet neutrophils collided with the wall at higher initial heights (see also Figure 6). At an initial height of 0.5 μm , spheroid contact times were about threefold longer than for corresponding neutrophils. Spheroid maximum contact areas were about 2–3-fold larger across the range of conditions. Larger contact areas and longer contact times are suggestive of a higher potential to form bonds that enable tethering and extravasation. Therefore, it is likely that neutrophils will form bonds at higher initial heights than spheroids. Longer axis lengths enable both neutrophils and spheroids to form bonds more readily than shorter lengths.

The effect of shear rate on collision TICA was studied for neutrophils and spheroids of length 1.9 at various starting heights (Figure 7c and d). The longest length was used throughout the remainder of the study to show the differences in behavior more markedly. Shear rates in the physiological range of 100–2000 s^{-1} were tested for initial heights ranging from 0.5–3 μm . In Figure 7, the TICA are shown for neutrophils (c) and spheroids (d). For both neutrophils and spheroids, contact time decreased as both shear rate and initial height were increased (Supplementary Figure 3a and c). However, the neutrophil TICA showed a concave down, decreasing trend while the spheroid TICA showed a concave up, decreasing trend. Although maximum contact area decreased as initial height was increased, all neutrophil and spheroid shear rates exhibited identical or near-identical behavior (Supplementary Figure 3b and d). As a result, TICA graphs displayed the same trend as contact time (Figure 7c and d). Comparing the neutrophil and spheroid geometries to one

another at the same conditions, spheroids experienced greater contact time, a greater maximum contact area, and greater TICA for lower initial heights. TICA is assumed to be a surrogate for binding potential, so one would expect that binding potential will be higher at lower shear rates and initial heights for both geometries. Although neutrophils can collide with the wall from higher initial heights than spheroids, binding potential appears to be higher for spheroids at lower initial heights.

Neutrophils experience higher contact force during collisions

In addition to TICA, increased contact force and contact pressure can contribute to greater binding potential. Figure 8a shows the average contact force and contact pressure (over the maximum contact area) for neutrophils and spheroids of varying cell length ratios (1.1–1.9) at an initial lowpoint of $R/8 = 0.5 \mu\text{m}$. The contact force and corresponding contact pressure are shown over time for a neutrophil and spheroid of length 1.3 in Figure 8b. In Figure 8a, the average contact force during collision increased for both neutrophils and spheroids as the length aspect ratio was increased. Neutrophils experienced higher contact force than corresponding spheroid lengths, and the rate of the increase of contact force over pseudopod length was greater than for spheroids. Conversely, spheroids experienced larger mean contact pressure than corresponding neutrophils. The average spheroid contact pressure exhibited biphasic behavior, increasing linearly from aspect ratio 1.3 through 1.7, then decreasing to length 1.9. The average neutrophil contact pressure increased with pseudopod length. Figure 8b displays the length 1.3 for neutrophil and spheroid collisions in greater detail. Maximum contact area remained constant throughout both collisions, so contact pressure and contact force curves follow the same shape. The neutrophil collision began slightly later in the trajectory than the spheroid collision and was about half the time duration. The contact force and pressure values for the spheroid simulation are nearly constant over time, increasing and then decreasing gradually through the collision. In contrast, the neutrophil contact force and pressure curves start with a slight increase, then a rapid increase to a higher value, then remain at the higher value. The sharpest increase occurred when the neutrophil was at its lowest point during the trajectory, while the pseudopod was pointing down into the steric layer.

The pseudopod is a “hotspot” of collision contact

A range of initial x , y , z angles were studied for a neutrophil with pseudopod and spheroid of length 1.9 placed at an initial lowpoint of $R/4$, where R is the hydrodynamic radius of $4 \mu\text{m}$. Angle combinations in the range of $\pi/18$ to π at intervals of $\pi/18$ for x , y , and z were examined (a total of 729 angles), and those angles for which the initial position would cause penetration of the wall were excluded. There were 323 angles analyzed for the neutrophil and 81 examined for the spheroid geometry. The initial height was chosen as a compromise between more frequent collision occurrence and with relatively fewer neutrophil positions excluded due to steric overlap with the wall. Histograms showing the frequency of contact times, contact areas, TICA, and maximum contact force during collisions for both geometries are shown in Figure 9. Contact time is spatially mapped on the cell surfaces in Figure 10. For the neutrophil, the histograms of contact time (Figure 9a) and TICA (Figure 9e) exhibited approximately Gaussian distributions, whereas contact area frequency (Figure 9c) displayed a bimodal distribution at about 4 and $8 \mu\text{m}^2$. This is due to the small number of

nodes that made contact with wall (Figure 10a). Thus, contact time contributed more variation to TICA than did maximum contact area. There were two principle areas of contact on the neutrophil, the tip of the pseudopod and the side of the body. Contact more frequently occurred on the pseudopod. In contrast, contact was observed over most of the spheroid's surface, with a larger hotspot near one end and a smaller hotspot on the other end (Figure 10b). The observed asymmetry is a consequence of the initial orientation of the cell. The contact time and TICA frequencies for the spheroid were skewed towards higher values. There was a greater range of maximum contact area (Figure 9d) and more nodes made contact with the wall (Figure 10b). The mean contact time and contact area for spheroids (shown in Figure 9b and Figure 9d) were greater than for neutrophils (Figure 9a and Figure 9c) by 27.8% and 31.6%, respectively. Consequently, the average TICA for spheroids was higher than for neutrophils (Figure 9g and h). Whereas contact is spread over most of the spheroid's surface, neutrophil contact is concentrated on the pseudopod tip and, to a lesser degree, on a spot on the spherical body. However, the average maximum contact force during collisions was slightly higher for neutrophils (Figure 9g) than for spheroids (Figure 9h), and there was a greater range of values. To summarize, the average contact time, contact area, and TICA are higher for spheroids than for neutrophils. However, the average maximum contact force exerted by the neutrophil on the wall during a collision is greater than for spheroids.

DISCUSSION

Pseudopods have a variety of functions for leukocytes: they aid in mobility, crawling, phagocytosis, and transport out of the blood vessels^{1,3,10,27,32}. Here we have shown that they may have the additional function of enabling the initial contact of free-flowing neutrophils with the endothelial wall, an event in the cascade that precedes cell arrest and extravasation. Pseudopods may then physically contribute to the progression of an inflammatory response. We found that at lower heights, longer pseudopods cause neutrophils to “pole vault” off of the endothelial surface and remain at a higher height thereafter, a phenomenon that has also been observed for oblate spheroid trajectories²². Our study showed that neutrophils with pseudopods have a higher likelihood of collision than equivalent prolate spheroids, but spheroids have a significantly higher TICA. However, neutrophils have the greatest contact on their pseudopod, and receptors are typically denser there than on the neutrophil body¹. Thus, the binding potential on the pseudopod may be higher than what might be assumed by considering only TICA. Pseudopod projections increase the contact area between neutrophils and the endothelium, and it was determined that longer pseudopods increased neutrophil collision frequency more than smaller pseudopods. Furthermore, longer pseudopods and lower shear rates increased TICA. A computational model by Zhao and colleagues suggests that longer microvilli are necessary for instigating tethered rolling but that lower stresses may have insufficient collisional contact force for tethering to occur³⁴. Our examination of mean collision contact force, another indicator of binding potential, indicated an increase with pseudopod length. At an initial gap of 0.5 μm between the cell and wall, neutrophils had higher mean contact force but lower contact pressure than spheroids due greater contact area. There exists a trade-off between the likelihood of collision and binding potential due to TICA and contact force with

neutrophil and spheroid geometries. However, the finding that pseudopods increase the collision frequency of and binding potential is consistent with evolutionary advantage, as neutrophils display features that help them extravasate out of blood vessels^{1,27,34}.

CONCLUSIONS

This work presents an analysis of the near-wall hydrodynamic collisions of a neutrophil geometry consisting of a spherical body with a Gaussian-shaped pseudopodial extension. During inflammation, neutrophil shape is critical in determining the rolling and tethering behavior that leads to extravasation through the endothelium. Neutrophil geometries with pseudopods of varying lengths were studied and compared to spheroids of equal major axis length and volume. Contact time and contact area between the surface of the cell and the wall are represented in the metric of TICA. Greater collision frequency, contact force, and TICA predict increases in binding potential as there are more opportunities to reach receptors and more time to form bonds. Longer pseudopods and lower shear rates increase the potential for forming bonds. At lower initial heights, colliding spheroids exhibited greater contact area with the wall, but neutrophils were able to make contact with the wall at higher initial heights, thus increasing their binding potential. The pseudopod was found to be a hotspot of binding potential on the neutrophil surface. Contact occurs at two locations on the neutrophil's surface, the side of the spherical body and at the tip of the pseudopod; contact is prolonged on the pseudopod tip. This paper is the first study to analyze the behavior of neutrophils with stable pseudopods in collisions with the endothelium and address the more general question of how cell shape affects wall contact under shear flow. Future studies should examine the effect of deformable cells and pseudopods.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.

Three-dimensional diagram of spherical neutrophil with pseudopodial extension under shear flow near the blood vessel wall, modeled as a semi-infinite plane. The major axis, centroid height, and lowpoint are shown.

Length (normalized)	Neutrophil	Prolate spheroid
1.1
1.3
1.5
1.7
1.9

Figure 2.

Neutrophil and prolate spheroid geometries analyzed in this study. The neutrophil has a spherical body with a Gaussian-shaped pseudopod extension. The normalized length is equal to the distance between the center of the spherical body and the pseudopod tip divided by the body radius. The spheroids have the same major axis length as their corresponding neutrophils. All neutrophil and prolate spheroid geometries studied have a volume equal to a sphere of radius 4 μm .

Figure 3.
Side view of rolling trajectories of a neutrophil (a) and spheroid (b) of length 1.9 at a shear rate 1000 s^{-1} and initial height 0.5 μm .

Figure 4.

Lowpoint trajectories over time for neutrophils (a, c) and spheroids (b, d) at various initial heights. Trajectories in which no collision occurred (a, b) are compared with collision cases (c, d). Time is nondimensionalized with the reciprocal shear rate, 10^{-3} s. Centroid height is nondimensionalized with the hydrodynamic radius, $R = 4 \mu\text{m}$.

Figure 5.

Centroid height trajectories as a function of time for neutrophils (a, c) and spheroids (b, d) at various initial heights. Trajectories in which no collision occurred (a, b) are compared with collision cases (c, d). Time is nondimensionalized with the reciprocal shear rate, 10^{-3} s. Centroid height is nondimensionalized with the hydrodynamic radius, $R = 4 \mu\text{m}$.

Figure 6. Comparison of collision occurrences for neutrophils and spheroids as a function of major axis length and initial height. The curves represent the highest initial heights at which neutrophils or spheroids collided with the wall. The diagonally-patterned areas represent conditions under which collisions occurred.

Figure 7.

Effect of initial height and cell length ratio (1.1–1.9) on time integral contact area for neutrophils (a) and spheroids (b) of different lengths. Effect of initial height and shear rate time integral contact area for neutrophils (c) and spheroids (d).

Figure 8.

Average contact force and contact pressure (a) for neutrophils and spheroids of varying cell length ratios (1.1–1.9) at an initial lowpoint of $R/8 = 0.5 \mu\text{m}$. Contact force and pressure of a collision are shown dynamically for a neutrophil and spheroid of length 1.3.

Figure 9.

Histograms of collision metrics for 323 initial orientation angles of neutrophils (a, c, e, g) and 81 angles for prolate spheroids (b, d, f, h) at an initial lowpoint of $R/4 = 1 \mu\text{m}$. The average value of each metric and its standard deviation are shown in each histogram.

Figure 10.

Colormap showing the spatial distribution of contact time on neutrophil (a) and spheroid (b) surfaces, pooled from the collisions of >80 initial orientation angles at an initial lowpoint of 1 μm . Red indicates high contact time, and blue indicates low contact time.