MULTIPARTICLE ADHESION OF DEFORMABLE CELLS

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The inflammatory response in the microvasculature is known to involve a cascade of events. Typically, one of the first steps is the margination of leukocytes towards the surface of the endothelium. Next, specific receptor-ligand adhesion molecules mediate the rolling of leukocytes along the endothelium. This may lead to firm arrest, additional recruitment,[1] and subsequent migration of leukocytes to the extravascular tissue in the region of infection or injury. While the role of molecular mediators and the hemodynamics of leukocyte adhesion and extravasation are more or less understood individually, the complex nonlinear interaction between these factors is less so. The fact that rolling is much more stable *in vivo* than in cell-free assays points to fundamental shortcomings in our current understanding of selectin- and integrin-mediated adhesion based on results, to date, obtained in model systems. The research discussed here advances theoretical understanding of adhesion by examining cell deformation in response to physiological states of stress. The fluid dynamic setting is the Stokes flow in half-space past one or more spherical cells. Deformation of the cell results from the surface traction exerted by the fluid onto the cell, and from adhesive bonds formed between the cell and surface. Additionally, cell-cell effects are captured. The computational approach is based on the completed, double-layer, boundary integral equation method (CDL-BIEM).[2] Up to this point, existing computational models for deformable leukocytes are deficient in one or more of the following areas. They assume a two-dimensional model, or they require the complete three-dimensional calculation of the surrounding fluid field, or they lack physical models for chemical adhesion, or multiparticle effects. Computational results with our viscoelastic deformation model for the leukocyte coupled with the Multiparticle Adhesive Dynamics (MAD) code[1] gives insight into our hypothesis that cell flattening stabilizes selectin- and integrin-mediated adhesion, and that down regulation of either neutrophil or surface adhesion receptors can disrupt this stabilization. Additionally, results from the computational approach will provide insight on a second hypothesis that cell flattening at higher shear stresses causes the insensitivity of E-selectin mediated rolling velocity to shear stress observed *in vivo*.

Keywords: leukocyte deformation, adhesion

References

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