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Incorporation of Surface Protrusion and Tether Extraction into a Numerical Model of Leukocyte Rolling on the Endothelium

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Summary

Leukocyte rolling on the endothelium is the first critical step of the inflammatory response. During the rolling process, surface protrusion and tether extraction from both leukocytes and endothelial cells (ECs) are very likely. Surface protrusion refers to the tent-like cellular surface deformation generated by the point pulling force exerted by the blood flow. Once this force exceeds a certain magnitude, the crossover force, a tether (a cylindrical membrane tube with nanometer diameter) is extracted. It has been shown recently that, cellular surface protrusion can be modeled by the three-parameter solid and tether extraction can be modeled by the power-law relationship between the pulling force and the tether growth velocity. However, these new models have not been incorporated into any computational study of leukocyte rolling. In this study, we proposed a modified constitutive relationship for tether extraction based on our direct measurement of the threshold force with the micropipette aspiration technique (the pulling force required at zero tether growth velocity). We also incorporated all the new experimental findings (i.e., surface protrusion from ECs, modified tether constitutive equation, and receptor linkage to the cytoskeleton) into our two-dimensional computational model of leukocyte rolling. We found that our model accurately simulated the crossover from surface protrusion to tether extraction when different cells were pulled by probes with different stiffness. More importantly, we found that whether tethers could be extracted simultaneously during leukocyte rolling was greatly influenced by the receptor linkage to the cytoskeleton. If the receptor linkage to the cytoskeleton is governed by similar kinetics, simultaneous tether extraction was more likely; otherwise, single tether extraction from either leukocyte or EC was more likely. Therefore, leukocytes and ECs may control leukocyte rolling stability by controlling their receptor and membrane binding kinetics to the cytoskeleton.

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