Title: Multiscale model of platelet tethering and adhesion: similarities with the leukocyte adhesion cascade

Session: Similarities/differences in MSM for various biological systems (immunology vs. thrombosis/hemostasis)

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Abstract:
The tethering of platelets on the injured vessel surface mediated by von Willebrand factor (VWF) – GPIbα bonds, as well as the interaction between flowing platelets and adherent platelets, are two key events that take place immediately following blood vessel injury. Interestingly, the capture and participation of platelets at an injury site shares many similarities with the leukocyte adhesion cascade that occurs during inflammation. First, both cell types collide with the vessel wall and begin to tether and roll, as mediated by protein receptors that are well suited with fast rates of association and dissociation. For both cell types a second class of receptors then takes over (primarily integrin family) and mediates firm adhesion. During this recruitment process both cell types will "activate" in response to exogenous chemical signals or mechanical signal transduction. By applying the biophysical insights gained from the more well-studied problem of leukocyte adhesion, we can formulate advanced models of platelet adhesion and function.

Platelet accumulation triggers the initiation of hemostasis, a defensive mechanism to prevent blood loss. To understand and predict this complex process, one must integrate experimentally determined information on the mechanics and biochemical kinetics of participating receptors over very small time frames (1-1000μs) and length scales (10-100 nm), to collective phenomena occurring over seconds and tens of microns. In the present study, a unique three dimensional multiscale computational model, platelet adhesive dynamics (PAD), is applied to elucidate the unique physics of (i) a non-spherical, disk-shaped platelet interacting and tethering onto the damaged vessel wall followed by (ii) collisional interactions between a flowing/rolling platelet with a downstream adherent platelet. By analyzing numerous simulations under different physiological conditions, we conclude that the platelet's unique spheroid-shape provides heterogeneous, orientation-dependent rolling behavior which enhances cell-wall interactions, and that platelet tethering efficiency and rolling velocity are not greatly affected by shear rate changes at lower physiological values (< 500 s^{-1}). Platelet-platelet near field interactions are critical for cell-cell communication during the initiation of microthrombi. The PAD model described here helps to identify the physical factors that control the initial stages of platelet capture during this process.