Dynamics of Microvillus Deformation in Rolling Leukocytes

Maria K. Pospieszalska[1] and Klaus Ley[1]

***Short Abstract* —P-selectin glycoprotein ligand-1 (PSGL-1) binding to P-selectin mediates leukocyte rolling under conditions of flow. PSGL-1 is expressed on leukocyte microvilli and can exert a pulling force that deforms the microvillus. Depending on the magnitude of the bond force, a microvillus can be extended, or a thin membrane cylinder (a tether) can be formed at the tip of the microvillus. Here we propose a Kelvin-Voigt viscoelastic material as an improved model for microvillus extension. Using a modified version of our Event-Tracking Model of Adhesion (ETMA), we demonstrate how P-selectin—PSGL-1 bonds shape microvillus deformation and rolling of neutrophils.**

***Keywords* — ETMA, microvillus extension, microvillus tether, microvillus deformation, leukocyte rolling, Kelvin-Voigt.**

I. Introduction

THERE has been a substantial effort to model microvillus deformation. Khismatullin and Truskey [1] assume a spring model for microvillus extension. Shao et al. [2] propose a spring model for microvillus extension and a viscous model for microvillus tether formation. The same method is adopted by Caputo and Hammer [3] and by Pawar et al. [4].

Here, we use the existing model for microvillus tether formation and propose a Kelvin-Voigt viscoelastic material as an improved model for microvillus extension. The proposed model is in good agreement with the experimental data of Shao et al. [2]. Using a modified version of our Event-Tracking Model of Adhesion (ETMA) [5], we conducted multiple simulations of neutrophil rolling at low shear (wall shear rate of 50/s, P-selectin site density of 150 molecules/μm^2). By directly comparing the microvillus deformation process with the lifetimes of load-bearing bonds of that microvillus, we demonstrate how P-selectin—PSGL-1 load-bearing bonds shape microvillus deformation during neutrophil rolling. Our study was intended to identify the patterns of microvillus deformation, distinguish the contributions of microvillus extension and tether formation, study the impact of deformable microvilli on leukocyte rolling, and compare our modeling results with experimental work studying human neutrophils in a flow chamber [6].

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[1]Division of Inflammation Biology,
La Jolla Institute for Allergy and Immunology, La Jolla, CA, USA.
E-mails: mpospieszalska@liai.org, klaus@liai.org.

II. Results

Our diagrams illustrate the process of microvillus elongation during neutrophil rolling, showing the segments of microvillus extension and tether formation, and indicating the action of the bonds causing the elongation effect. The corresponding microvillus bond force, cell displacement, and cell translational velocity are also shown.

Under conditions studied we find that

- in general, a microvillus with a higher number of load-bearing bonds develops a longer extension/tether,
- on average, the microvillus extension constitutes 65% of the total microvillus-tether complex extension,
- compared to the corresponding model with non-deformable microvilli, the mean duration of the load-bearing state for bonds of deformable microvilli significantly increases by 54%, and the translational velocity of rolling leukocytes decreases by 35%,
- a rolling cell with deformable microvilli is in motion even while P-selectin—PSGL-1 bonds exist.

II. Conclusion

Compared to previous efforts aimed at modeling extensible microvilli, the Kevin-Voigt model more realistically matches data obtained in micropipette experiments of [2]. Our modeling demonstrates diverse microvillus deformation activities at a wall shear rate of 50/s, whereas Schmidtke and Diamond [7] detected no tethers in their experiments at wall shear rates of 50/s and below, presumably because of limitations in the spatial and temporal resolution of available experimental techniques. Conceptually, our model agrees with experimental results obtained in flow chamber studies [6] that suggest a stabilizing effect of extensible microvilli, although the experimental work was conducted at higher shear rates.

References

[1] Khismatullin DB, Truskey GA. (2005). *Phys. Fluids* **17**:031505.1-031505.21.
[2] Shao JY, Ting-Beall HP, Hochmuth RM. (1998). *Proc. Natl. Acad. Sci.* **95**:6797-6802.
[3] Caputo KE, Hammer DA. (2005). *Biophys. J.* **89**:187-200.
[4] Pawar P, et al. (2008). *Am. J. Physiol. Heart Circ. Physiol.* **295**: H1439-H1450.
[5] Pospieszalska MK, et al. (2009). *Microcirculation* **16**:115-130.
[6] Park, EYH, et al. (2002). *Biophys. J.* **82**:1835-1847.
[7] Schmidtke DW, Diamond SL. (2000). *J. Cell Biol.* **149**: 719-729.