Biophysical Journal, Volume 99

Supporting Material

A Semi-Analytical Model to Study the Effect of Cortical Tension on Cell Rolling

Suman Bose, Sarit K. Das, Jeffrey M. Karp, and Rohit Karnik

A) Three-element model of microvillus

In order to model the dynamical response of the microvillus, we used a three element model as described in the paper. Briefly, the model consists of a spring (stiffness K_m) and damper (viscosity η_m) in series, which are both in parallel to another spring (stiffness K_c). Transition to viscous regime occurs when the force in the spring K_c exceeds the critical force F_0, in which case the force in that spring is held constant at F_0. The governing equations are:

$$\begin{aligned} &\frac{dF_m}{dt}+\frac{K_m}{\eta_m}F_m=\frac{K_cK_m}{\eta_m}l+\left(K_c+K_m\right)\frac{dl}{dt} && \text{for } K_cl\le F_0 \\ &\frac{dF_m}{dt}+\frac{K_m}{\eta_m}\left(F_m-F_0\right)=K_m\frac{dl}{dt} && \text{for } K_cl>F_0 \end{aligned} \tag{1}$$

When a constant force is applied such that the extension doesn't cause microvillus transition to the viscous regime, the steady state extension is governed by the spring stiffness K_c. In another scenario, when a constant force is applied such that it causes transition to the viscous regime, the steady state dynamics are governed purely by the viscous damper (η_m) as the microvillus would extend at a constant velocity given by $\vartheta=(F-F_0)/\eta_m$. In micropipette experiments, Shao et al. (1) applied a constant force on neutrophils and recorded microvillus extensions. From the steady state response they predicted an elastic stiffness of 43 pN/μm and a viscosity of 11 pN-s/μm, which for our model are assigned to K_c and η_m respectively. Recently, Xu et al. (2) used an optical trap to extract microvilli from neutrophils up to a fixed distance and studied their relaxation behavior. We used their data to estimate the value of K_m. The optical trap was modeled by a Kelvin-Voigt model with a spring (80 pN/μm) placed in parallel to a damper (0.32 pN-s/μm) as described by Xu (2). The Kelvin-Voigt body was connected in series to the three-element microvillus and the combined system of equations was solved numerically. We found a good agreement between the simulated results and the experimental data for K_m=200 pN/μm. Figure S1 shows the comparison between the results from the model and the experimental data available.

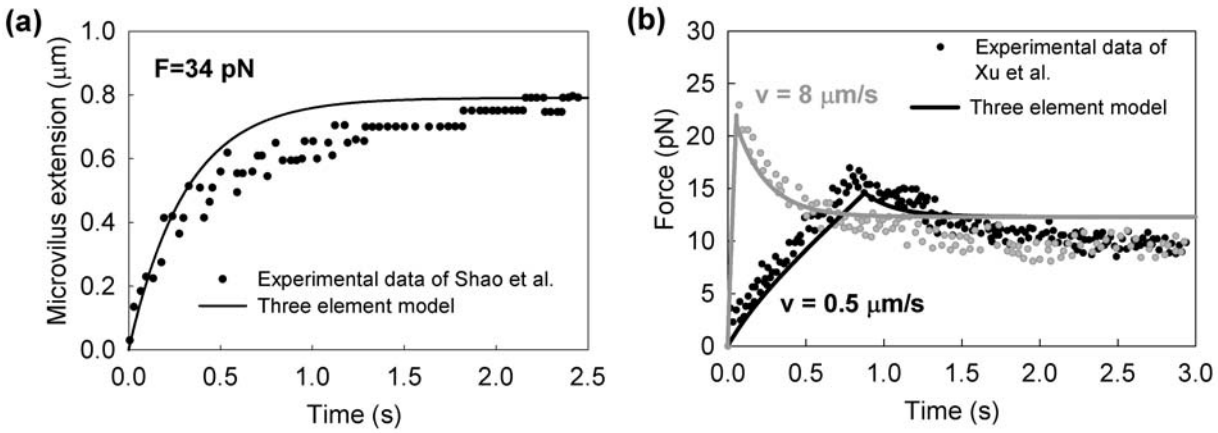

Figure S1: (a) Extension of microvillus under a constant force of 34 pN was simulated using the three-element model and compared to the micropipette aspiration data of Shao et al. (1). The experimental data were corrected for time and natural length of microvillus such that t=0 represented the beginning of the extension process. (b) Comparison between the microvillus relaxation data by Xu et al. (2) and the prediction of the model (for K_m=200 pN/μm). In the experiments, microvilli were pulled to a fixed distance with a certain velocity and then held in place, and the decay in force was noted. Different rates of pulling, shown in different colors (grey and back), gave different transient responses.

B) State diagram of rolling for varying on-rates and off-rates of receptor ligand interaction

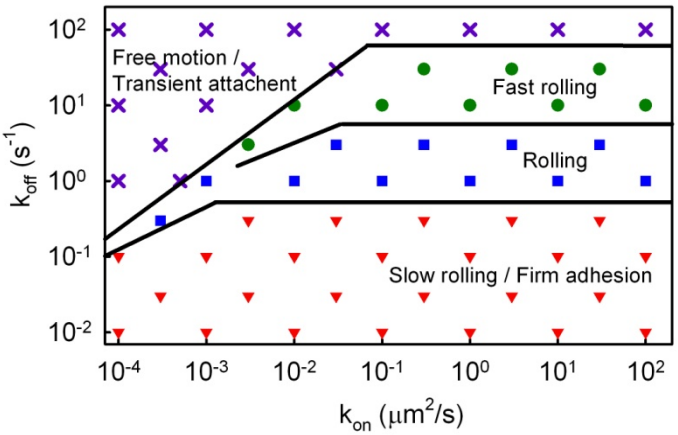

Figure S2: The state space diagram for rolling for different on and off rates of the receptor ligand interactions. The shear stress was 1 dyn/cm^2, ligand density was N_L=50 μm^{-2} and membrane tension was T_c=24 pN/μm. Three regimes - slow rolling (or firm adhesion), rolling and fast rolling were identified based on the ratio of rolling velocity to hydrodynamic velocity as described in the main text. Free motion or transient tethering denotes the region where the equations did not yield a solution, indicating that steady rolling was not feasible. k_{off} significantly affected cell rolling, indicating that bond breakage rate is a crucial parameter that dictates the state of rolling. Stronger bonds (lower k_{off}) resulted in higher force carried per bond reducing the rolling velocity. On the contrary, k_{on} had an effect on the rolling state only at low values (< 0.1 μm^2/s) indicating a regime where bond formation is compromised. In this regime the lower formation rate of the bonds had to be compensated by a lower breakage rate to ensure

steady rolling resulting in the dip of the rolling region observed in the on-off diagram. All other parameters are as listed in Table 1 (main text).

C) Dependence of the state space diagram on cortical tension

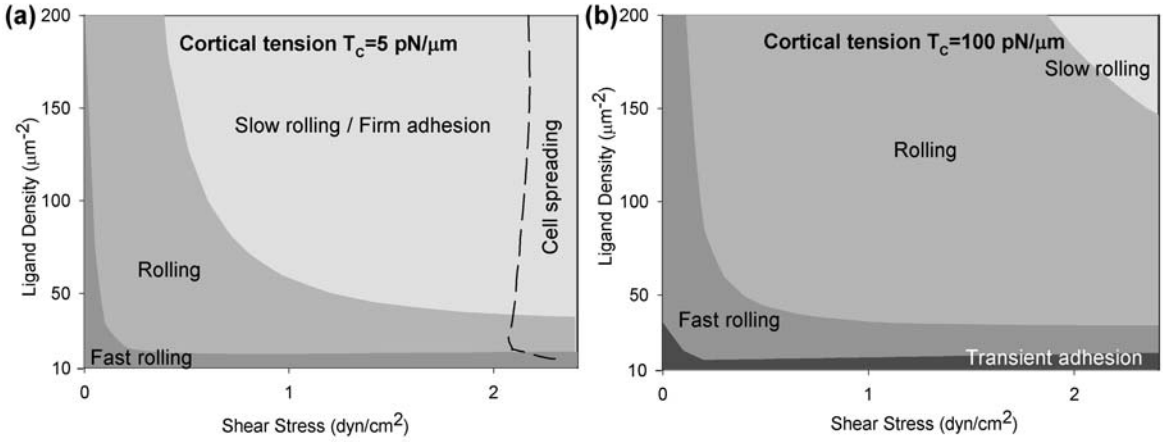

Figure S3: The state space diagram in the case of low (5 pN/μm) cortical tension (a) exhibits cell spreading at low shear stress in the range of 2 dyn/cm^2 and slow rolling/firm adhesion at relatively low ligand densities and shear stresses compared to the case of high (100 pN/μm) cortical tension (b).

References

1. Shao, J. Y., H. P. Ting-Beall, and R. M. Hochmuth. 1998. Static and dynamic lengths of neutrophil microvilli. Proceedings of the National Academy of Sciences of the United States of America 95:6797-6802.
2. Xu, G., and J. Y. Shao. 2008. Human neutrophil surface protrusion under a point load: location independence and viscoelasticity. American Journal of Physiology-Cell Physiology 295:C1434-C1444.