On the role of passive and active cytoskeleton forces in shape determination, function and dynamics of cells

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Protrusions at the leading-edge of a cell play an important role in cellular spreading and motility. However, the physics of the cell motility is still not well understood. We present a combined theoretical and experimental study of the cell movement on the surface of different geometry as well as the mechanism of efficient phagocytosis and the mechanism of coiling of cellular protrusions around fibers. Our theoretical model describes the membrane leading-edge that are produced by curved membrane proteins that recruit the protrusive forces of actin polymerization, and identifies the role of bending and adhesion energies. Among other our model recovers the observed cell migration on the sinusoidal substrate, where cells move along the grooves (minima), while avoiding motion along the ridges. Further we predicted in accordance with experimental results that the cell's leading-edge may coil on fibers with circular cross-section (above some critical radius), but the coiling ceases for flattened fibers of highly elliptical cross-section. We also considered the phagocytosis of spherical and non-spherical particles and found that non-spherical particles are more difficult to engulf in comparison to the spherical particles of the same surface area. For non-spherical particles, the engulfment time crucially depends on the initial orientation of the particles with respect to the vesicle. Our model also offers a mechanism for the spontaneous self-organization of the actin cytoskeleton at the phagocytic cup, in good agreement with recent high-resolution experimental observations.

References:

1.R.K. Sadhu, M. Luciano, W. Xi, C. Martinez-Torres, M. Schröder, C. Blum, M. Tarantola, S. Villa, S. Penič, A. Iglič, C. Beta, O. Steinbock, E. Bodenschatz, B. Ladoux, S. Gabriele, Nir S. Gov: A minimal physical model for curvotaxis driven by curved protein complexes at the cell's leading edge. *Proceedings of the National Academy of Sciences* (PNAS) 121 (12): e2306818121, 2024.

2. R.K. Kumar Sadhu, C. Hernandez-Padilla, Y.E. Eisenbach, S. Penič, L. Zhang, H.D. Vishwasrao, B. Behkam, K. Konstantopoulos, H. Shroff, A. Iglič, E. Peles, A. S. Nain, N. S. Gov: Experimental and theoretical model for the origin of coiling of cellular protrusions around fibers. *Nature Communications* 14: 5612, 2023.

3. R.K. Sadhu, S. R. Barger, S. Penič, A. Iglič, M. Krendel, N.C. Gauthiere, N.S. Gov: A theoretical model of efficient phagocytosis driven by curved membrane proteins and active cytoskeleton forces. *Soft Matter* 19, 31-43, 2023.

4. R.K. Sadhu, A. Iglič, N. S. Gov: A minimal cell model for lamellipodia-based cellular dynamics and migration. *Journal of Cell Science* 136 (14): jcs260744, 2023.

5. R.K. Sadhu, S. Penič, A. Iglič, N. S. Gov: Modelling cellular spreading and emergence of motility in the presence of curved membrane proteins and active cytoskeleton forces. *Eur. Phys. J. Plus* 136:495, 2021.