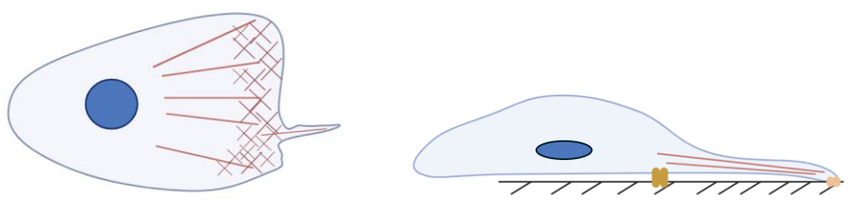
A Multiscale approach to study the mechanisms of filopodia mechanotransduction and their role in guiding cell motility

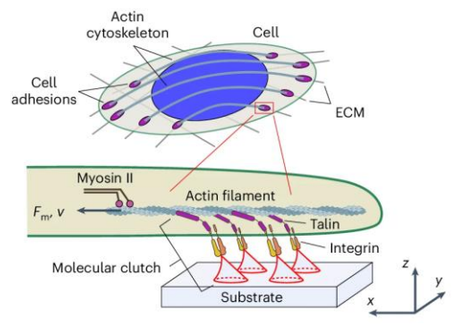
Qiuyu Wang[1,3], Mingxi Yao[2], Heath E. Johnson[3], Artem K. Efremov[1]

1. Institute of Systems and Physical Biology, Shenzhen Bay Laboratory, Shenzhen, China 518132
2. Department of Biomedical Engineering, Southern University of Science and Technology, Shenzhen, China 518055
3. School of Biological Sciences, The University of Hong Kong, Hong Kong SAR, China 999077

Introduction

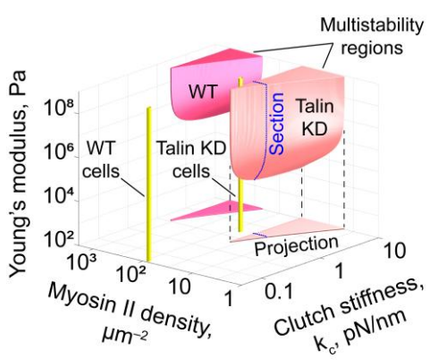


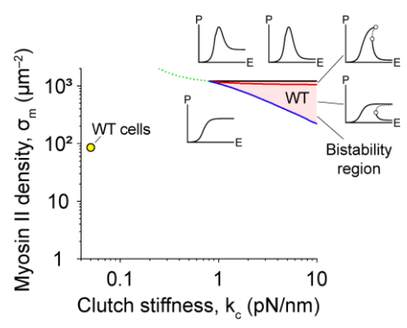
Cells use filopodia to probe extracellular matrix stiffness and initiate the formation of cell adhesions



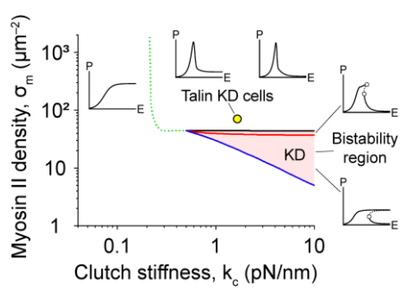
The model can predict diverse dynamic behaviours of cell-adhesion complexes

- The rate of molecular-clutch formation
- Adaptor protein elasticity
- Myosin II density



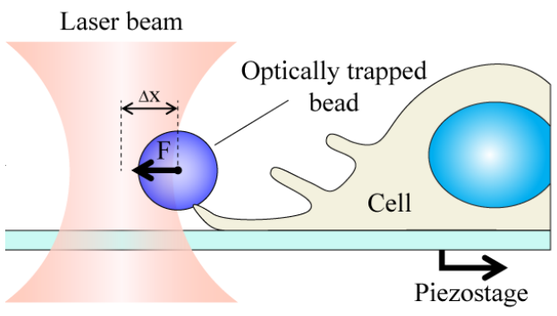


The values of the myosin II density and the rigidity of the intracellular part of molecular clutches can strongly influence cell behaviour

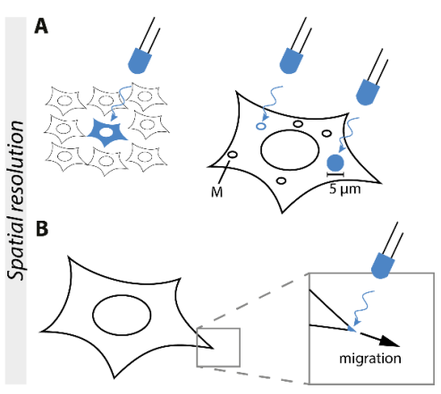


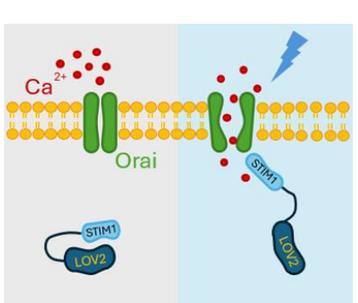
Methods

Optical tweezer to apply external mechanical force

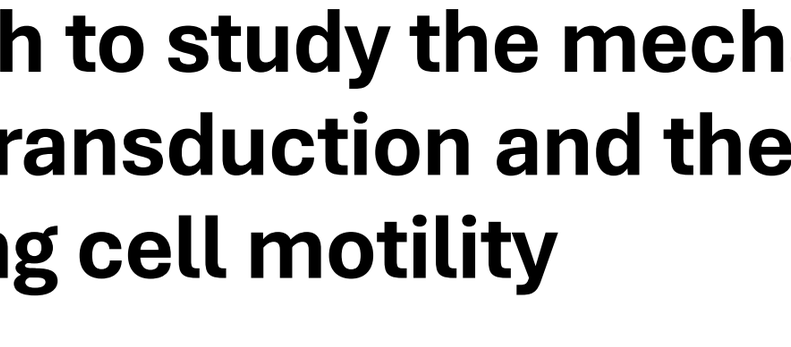


Optogenetics to give light stimulation making calcium channels open

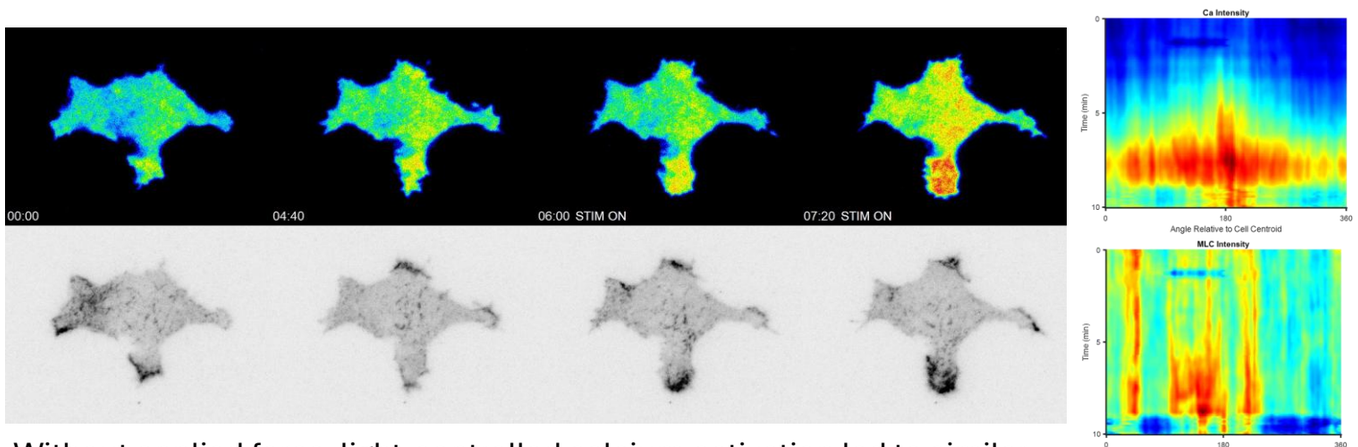




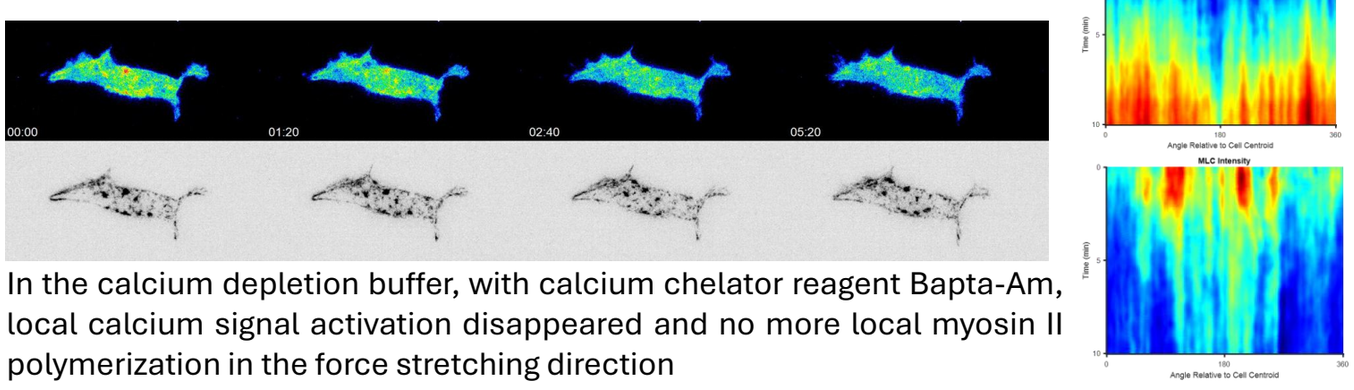
Results



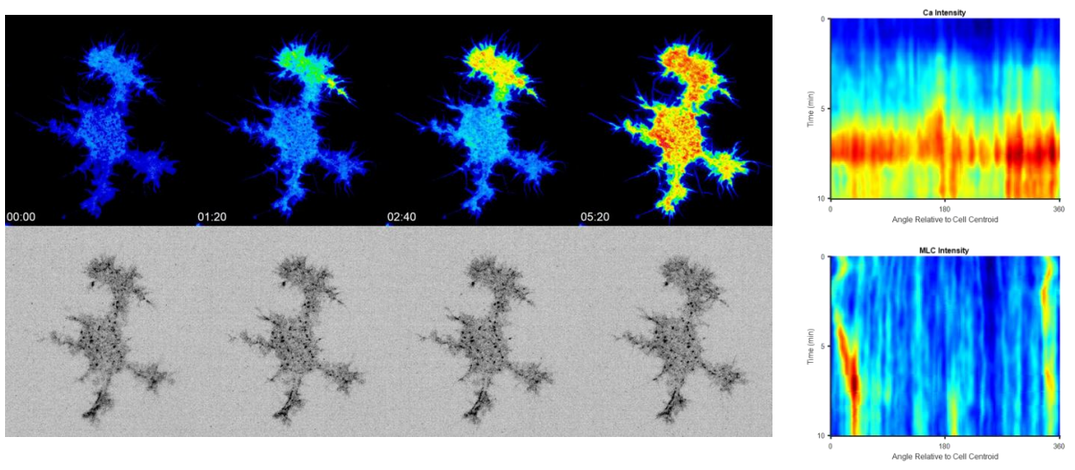
Force-induced calcium activation caused the myosin II polymerization towards the force-pulling direction



Without applied force, light-controlled calcium activation led to similar myosin II polymerisation

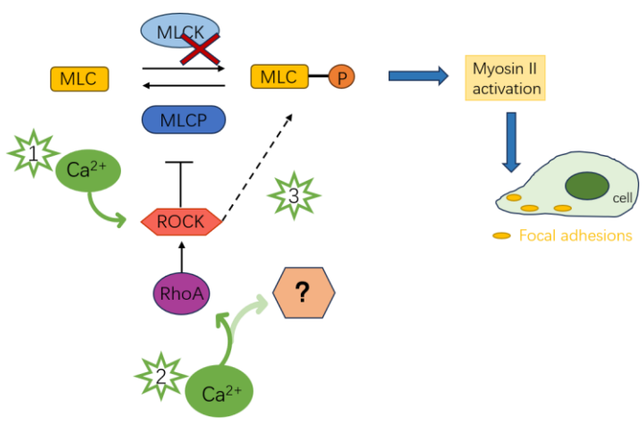


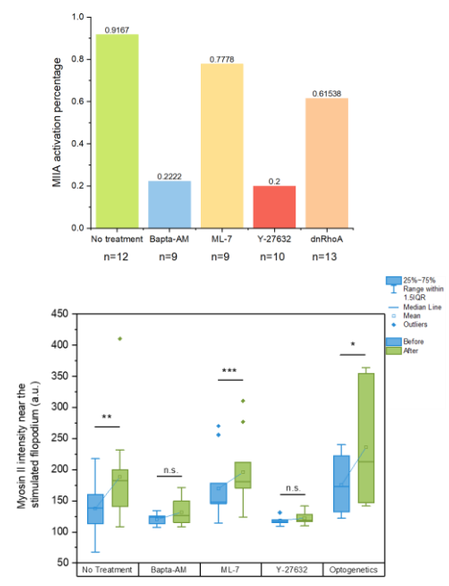
In the calcium depletion buffer, with calcium chelator reagent Bapta-Am, local calcium signal activation disappeared and no more local myosin II polymerization in the force stretching direction



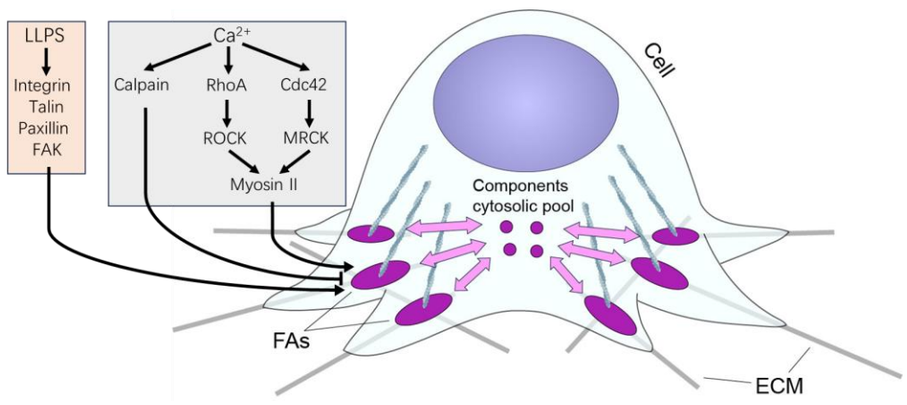
Myosin II polymerization was blocked in the direction of stretching force with the Rho-associated protein kinase (ROCK) inhibitor Y-27632

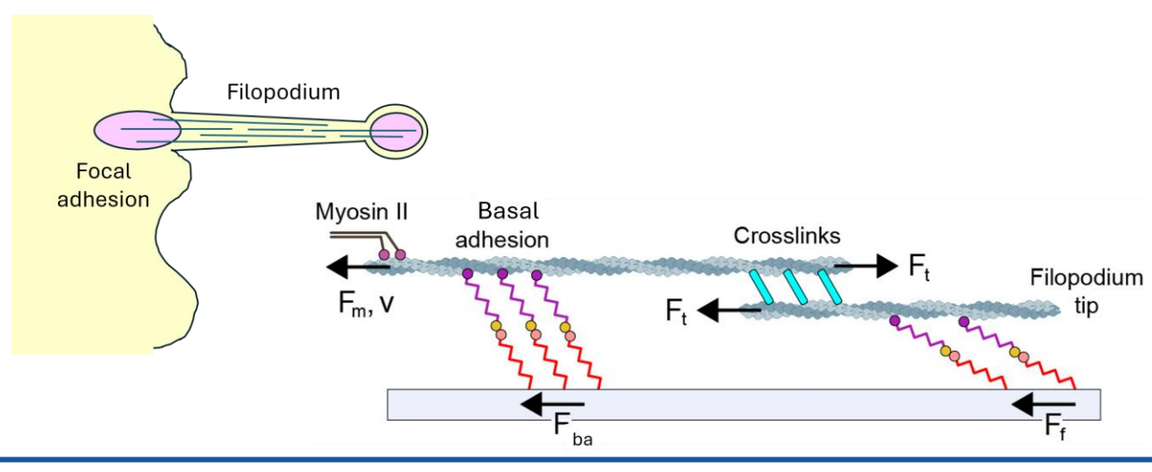
Summary





Model





Reference

1. Efremov, A.K., Yao, M., Sun, Y., Tee, Y.H., Sheetz, M.P., Bershadsky, A.D., Martinac, B., and Yan, J. (2022). Application of piconewton forces to individual filopodia reveals mechanosensory role of L-type Ca(2+) channels. Biomaterials 284, 121477. 10.1016/j.biomaterials.2022.121477.
2. Kramer, M.M., Lataster, L., Weber, W., and Radziwill, G. (2021). Optogenetic Approaches for the Spatiotemporal Control of Signal Transduction Pathways. Int J Mol Sci 22. ARTN 5300 10.3390/ijms22105300.