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Studying neuronal biomechanics and its role in CNS development KRISTIAN FRANZE, HANNO SVOBODA, University of Cambridge, UK, LUCIANO DA F. COSTA, University of Sao Paulo, Brazil, JOCHEN GUCK, CHRISTINE HOLT, University of Cambridge, UK — During the development of the nervous system, neurons migrate and grow over great distances. Currently, our understanding of nervous tissue development is, in large part, based on studies of biochemical signaling. Despite the fact that forces are involved in any kind of cell motion, mechanical aspects have so far rarely been considered. Here we used deformable cell culture substrates, traction force microscopy and calcium imaging to investigate how neurons probe and respond to their mechanical environment. While the growth rate of retinal ganglion cell axons was increased on stiffer substrates, their tendency to grow in bundles, which they show *in vivo*, was significantly enhanced on more compliant substrates. Moreover, if grown on substrates incorporating linear stiffness gradients, neuronal axons were repelled by stiff substrates. Mechanosensing involved the application of forces driven by the interaction of actin and myosin II, and the activation of stretch-activated ion channels leading to calcium influxes into the cells. Applying a modified atomic force microscopy technique *in vivo*, we found mechanical gradients in developing brain tissue along which neurons grow. The application of chondroitin sulfate, which is a major extracellular matrix component in the developing brain, changed tissue mechanics and disrupted axonal pathfinding. Hence, our data suggest that neuronal growth is not only guided by chemical signals – as it is currently assumed – but also by the nervous tissue's mechanical properties.

Kristian Franze
University of Cambridge, UK

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