Matrix elasticity gradients guide neuronal polarity by controlling microtubule network mobility

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Neuronal polarization and axon specification depend on extracellular cues, intracellular signaling, cytoskeletal rearrangements and polarized transport, but the interplay between these processes has remained unresolved. The polarized transport of kinesin-1 into a specific neurite is an early marker for axon identity, but the mechanisms that govern neurite selection and polarized transport are unknown3,4. Here we show that extracellular elasticity gradients can control polarized transport and axon specification, mediated by Rho-GTPases whose local activation is necessary and sufficient for polarized transport. Selective Kinesin-1 accumulation furthermore depends on differences in microtubule network mobility between neurites and local control over this mobility is necessary and sufficient for proper polarization, as shown using optogenetic anchoring of microtubules. Together, these results explain how mechanical cues can instruct polarized transport and axon specification.