Short-range propagation of plasma membrane tension in neurons facilitated by periodic barriers

In two types of roundworm neurons that can sense mechanical stimuli, the tension in the plasma membrane propagates rapidly, but it is spatially confined by periodic barriers formed by cytoskeletal and membrane proteins. This spatial restriction enables localized mechanical signalling, enhancing a neuron's capacity to process multiple stimuli independently.

This is a summary of:
Català-Castro, F. et al. Obstacles regulate membrane tension propagation to enable localized mechanotransduction. *Nat. Phys.* https://doi.org/10.1038/s41567-025-03037-x (2025).

Published online: 03 November 2025

The question

A major goal in the field of mechanobiology is to understand how physical stimuli are converted into biochemical signals (that is, mechanotransduction). However, our knowledge about how cells respond to mechanical stimuli and how mechanical stresses distribute within cells is incomplete. A more detailed picture of the frequency-dependent, non-homogeneous, and anisotropic (direction-dependent) material properties of cells would facilitate our understanding of many processes in mechanobiology, for example, how embryos develop, how the cortex of the mammalian brain folds and how we sense touch at our fingertips. Because many known molecular force sensors are transmembrane proteins, tension gradients in the plasma membrane are thought to regulate mechanoreceptor activity and mechanotransduction[1]. However, even this basic understanding of how mechanical stresses distributes within plasma membranes has recently been disputed[2]. The rheological properties of the membrane (how it deforms and flows under stress) are therefore important to determine which stimuli are transmitted and how far. Here, we revisit the mechanical properties of membrane in two different types of mechanosensory neurons to shed light on how mechanical stresses might be transmitted across the membrane.

The discovery

We used the well-studied touch receptor neurons and proprioceptors (sensory receptors that receive stimuli from within the body) from the roundworm *Caenorhabditis elegans*[3]. We developed a dual tether extrusion assay using two optical traps. Optical traps are highly focused laser beams that can measure force and manipulate microscopic objects. We used them to pull two lipid tethers out of the long axons (the sensory projections of the neurons). After forming the two tethers (Fig. 1a) on the same axon, we actively pulled on one tether, while recording the response on the second, passive tether (Fig. 1b). We optimized the system and confidently measured forces and dynamics with picoNewton accuracy. To guide the interpretation of the experimental results, we established a 3D finite element model that was based on the mechanical properties of the membrane and calculated how quickly mechanical information was dissipated through interactions with membrane-embedded obstacles, such as ion channels, cell adhesion molecules or other membrane proteins.

For both mechanoreceptor types, the propagated tension dropped exponentially with the distance from the perturbation, but it did so faster in the proprioceptors than in the touch receptors. We dissected the molecular signature of what limited the propagation of the tension using an array of genetic and pharmacological perturbations. Intriguingly, our experimental and theoretical analyses support a scenario in which periodically arranged obstacles, or struts, favour tension propagation at short distances, whereas randomly arranged obstacles favour tension propagation over long distances. Because most, if not all, neurons possess a periodic cytoskeleton (in which the associated membrane proteins are organized in repeated clusters)[4], our observation is likely to be a conserved and fundamental feature.

The implications

Restricting membrane tension propagation enables cells to confine mechanical responses to specific subcellular domains. This property enables precise, localized mechanotransduction without affecting the entire cell, which is crucial in neurons or polarized cells (where spatial segregation of function is essential) and might enhance the neuron's ability to encode complex mechanical information, contributing to fine-tuned sensory processing or adaptive motor responses. Indeed, in proprioceptors, which provide local output to motor neurons, limited tension spread might refine the mechanoresponse[3].

Applying force via optical traps is an artificial approach and likely to generate tension gradients and deformations that are highly exaggerated compared with natural stimuli (a touch or limb movement), which also engage the mechanics of the cytoskeleton and the extracellular matrix. Thus, our study might not fully reproduce the complexity or variability of endogenous mechanical inputs. Although mechanosensitive channels or cytoskeletal components are implicated in mechanotransduction, this work doesn't fully establish causality between specific structural features and functional outcomes, like signal transduction or behaviour.

The next steps are to incorporate the molecular identity of the primary barriers to tension propagation on the outside of the axon, such as cell adhesion molecules and the extracellular matrix. We also wish to study how the propagated tension couples to individual ion channels or adhesion receptors to visualize exactly where and how force is transduced at the molecular level.

Michael Krieg[1] & Padmini Rangamani[2]
[1]ICFO - Institut de Ciencies Fotoniques, Castelldefels, Spain. [2]University of California, San Diego, San Diego, CA, USA

EXPERT OPINION

This is a very timely paper. Given the important part that membrane tension has been shown to play in the regulation of cell function, it is very important to understand how localized this parameter is or how far it propagates. This information has considerable implications for the understanding of mechanotransduction. **Eva Kreysing, University of Cambridge, Cambridge, UK**

FIGURE

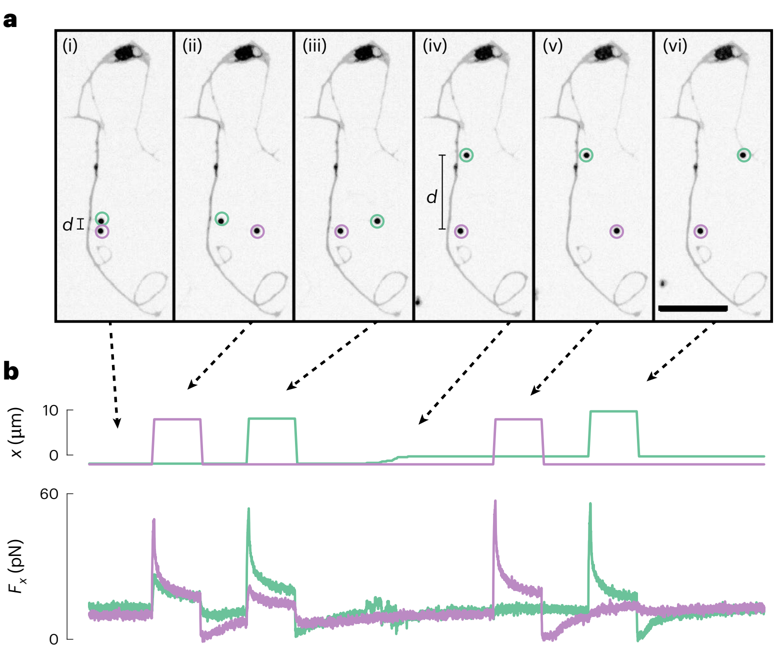

Fig. 1 | Measuring tension propagation using dual tether extrusion assay. a, Representative sequence of the tension propagation experiment. Two traps are tethered to an axon by means of a single membrane lipid nanotube. Pulling of the active trap (purple circle) causes a tension gradient that propagates into the axon and is perceived also by the second, passive trap (green circle). Then, the distance (*d*) between the two tethers is increased and the sequence is repeated. Scale bar, 20 μm. **b**, Corresponding distance between the two traps (top) and force profiles (bottom) of the active and the passive traps, indicating tension propagation along the axon. © 2025, Català-Castro, F. et al., CC BY-NC-ND 4.0.

BEHIND THE PAPER

We have long been interested in how mechanical signals activate neurons during touch and proprioception. During our past work focused on the cytoskeleton, we began to wonder whether the plasma membrane could support the transfer of mechanical information through physiologically meaningful distances. This curiosity was sparked by controversial and inconsistent reports in the recent literature, and thus it started as a side project, which has never gotten any major funding. Whereas the experiments themselves were relatively easy to perform, the most difficult part of the study was to bring the various observations into a common framework. A breakthrough came when the 3D modelling approach enabled us to reproduce the data and revealed that the spatial arrangement of membrane obstacles strongly shapes tension propagation. **M.K. & P.R.**

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FROM THE EDITOR

This work by Català-Castro, Bonilla-Quintana and co-workers stood out to us because it analyses in detail how fast membrane tension propagates and how localized it is. The overall aim is to understand mechanotransduction in cellular membranes, and with this study we are one step closer. **Editorial Team, *Nature Physics***