Bending compliance of lipid bilayer regulates the curvature threshold and pathway of membrane structural stability loss

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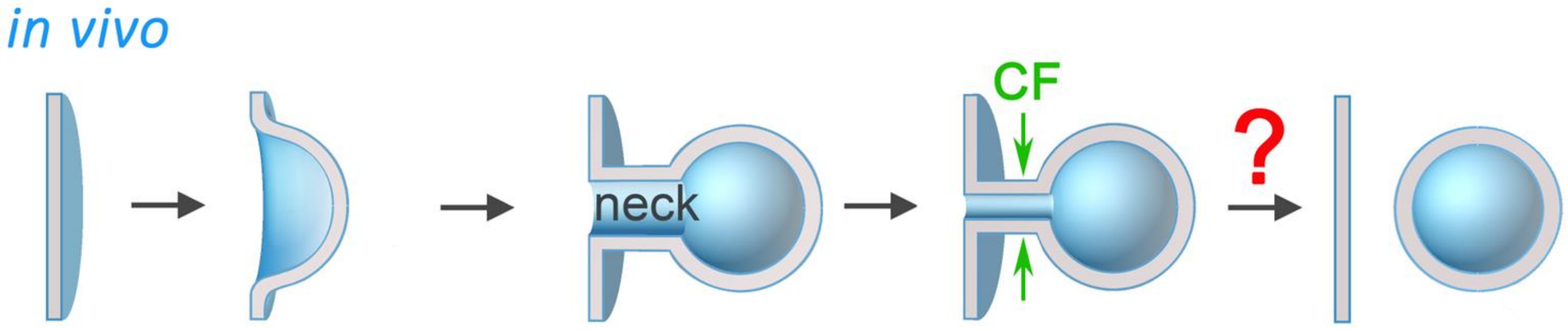
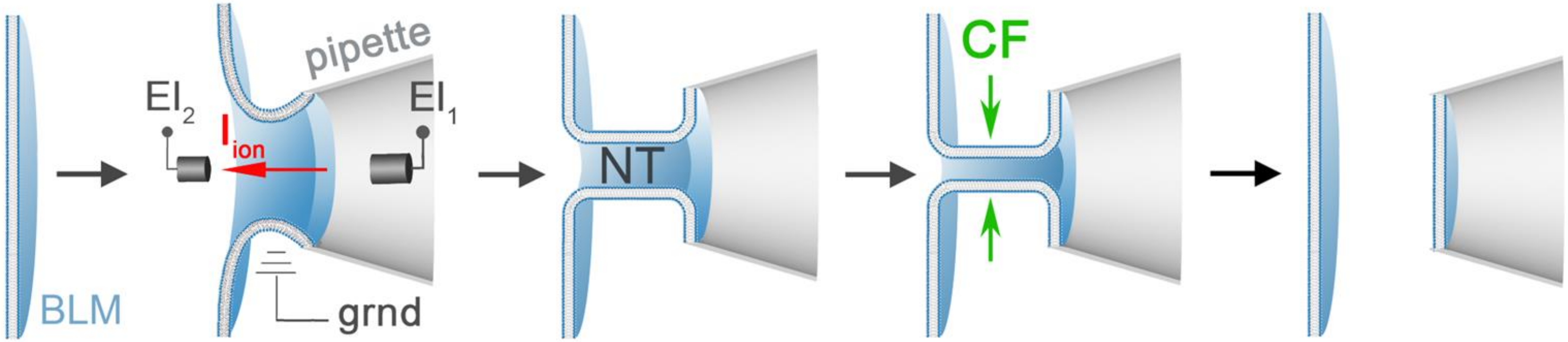
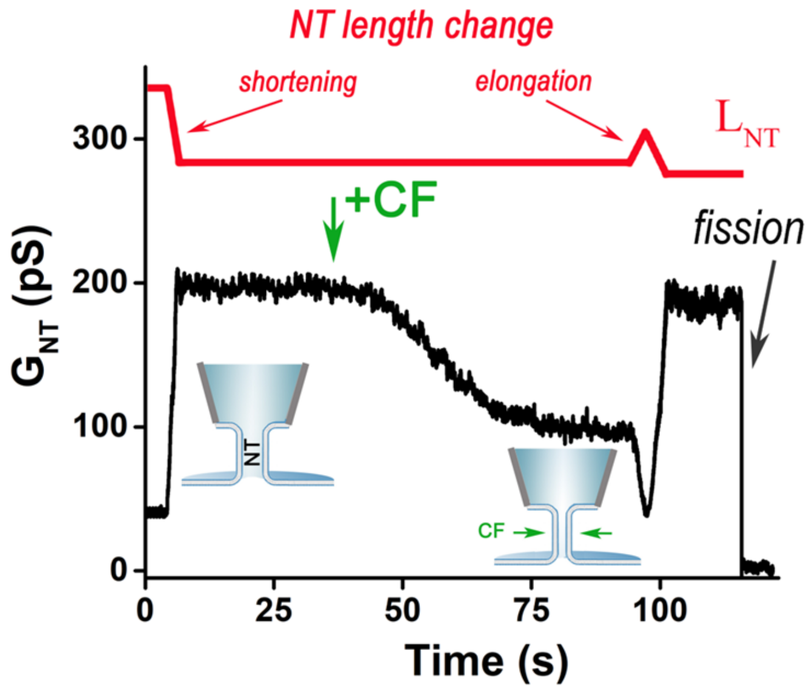
High curvature provokes a loss of structural stability of the lipid bilayer.

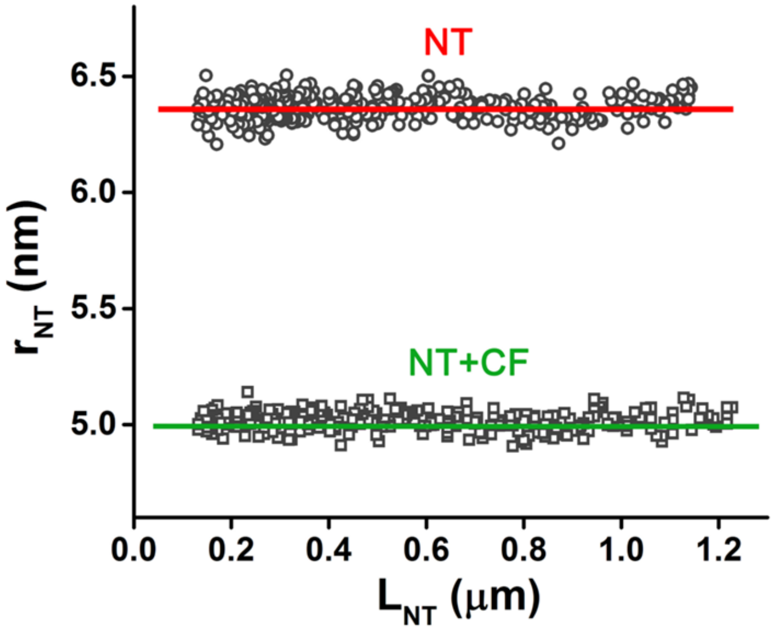


Division of a fluid compartment is a phenomenon equally frequent and important in life and technology. Starting as a macroscopic transformation, it ultimately scales down to a nanoscopic neck. To undergo scission, the fission neck must first scale down through a process termed constriction, during which the neck´s size decreases with its radius. Curvature stress may contribute to the formation of fission intermediates, but it remains unclear how. Indeed membrane stress has never been measured in fission intermediates in the context of membrane instabilities, so we don’t know whether defect nucleation also yields membrane stress.

Reconstruction of geometry of cellular membrane necks via pulling ultra-short lipid nanotubes (NT) from planar lipid bilayers

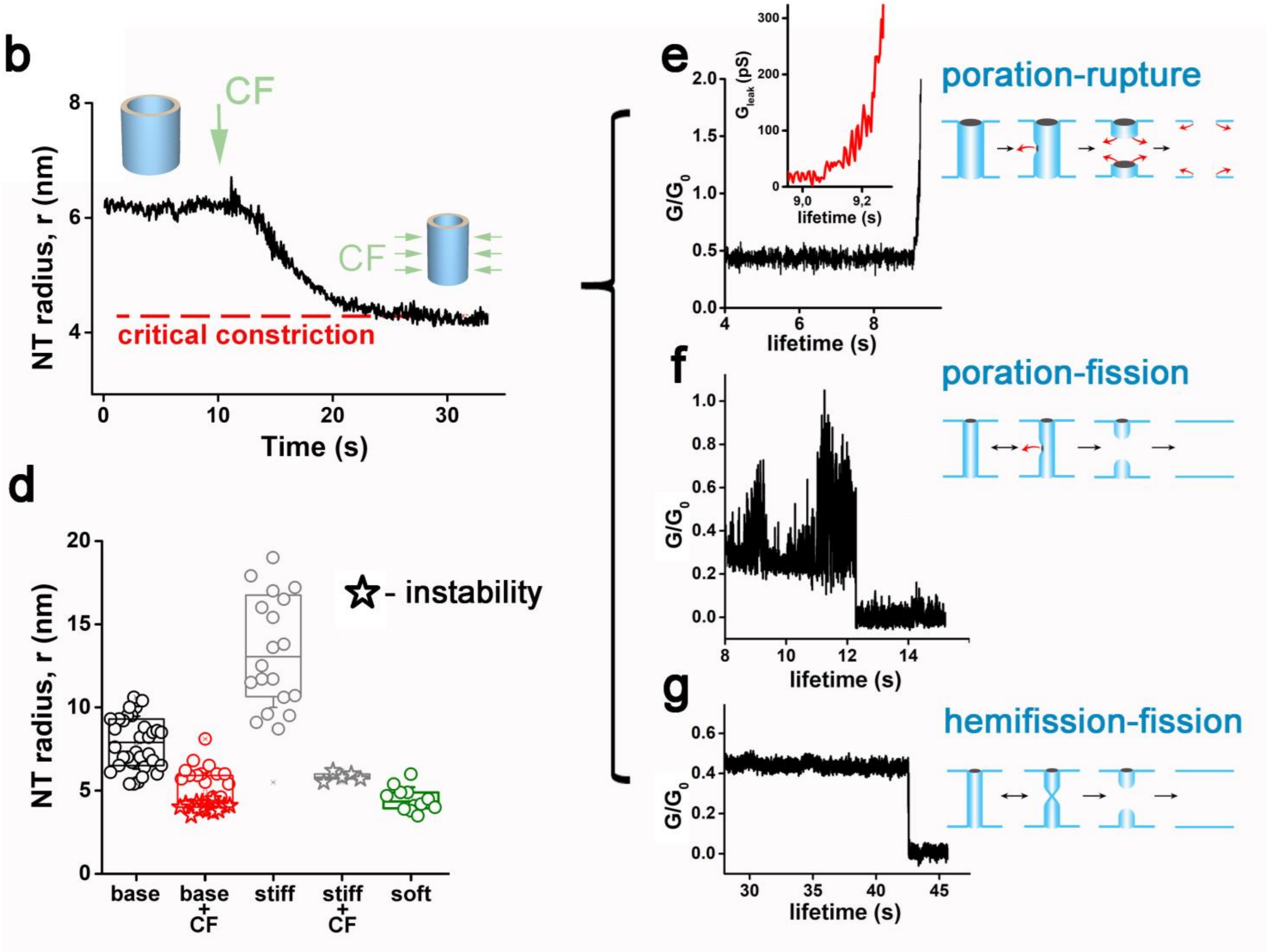






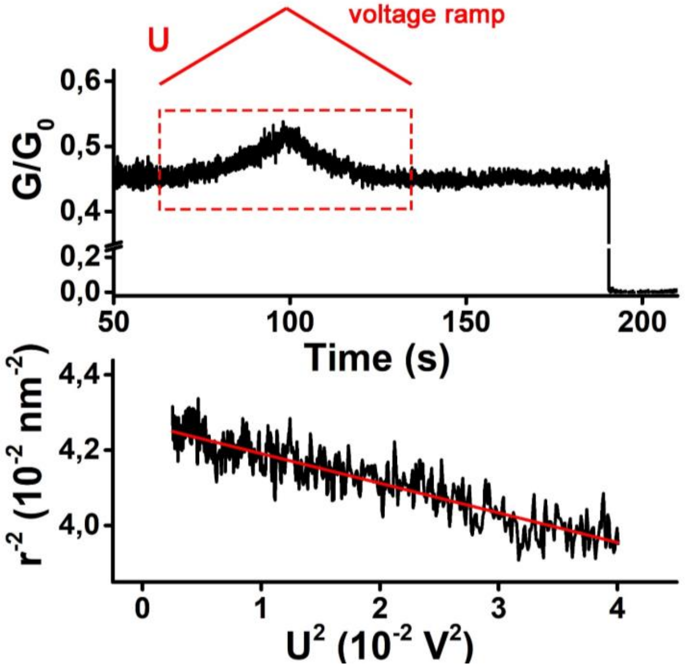
We measure ion current flowing through the lumen of electrically biased NT.

Topological reorganization of a membrane of a constricted NT reveals different pathways of remodeling

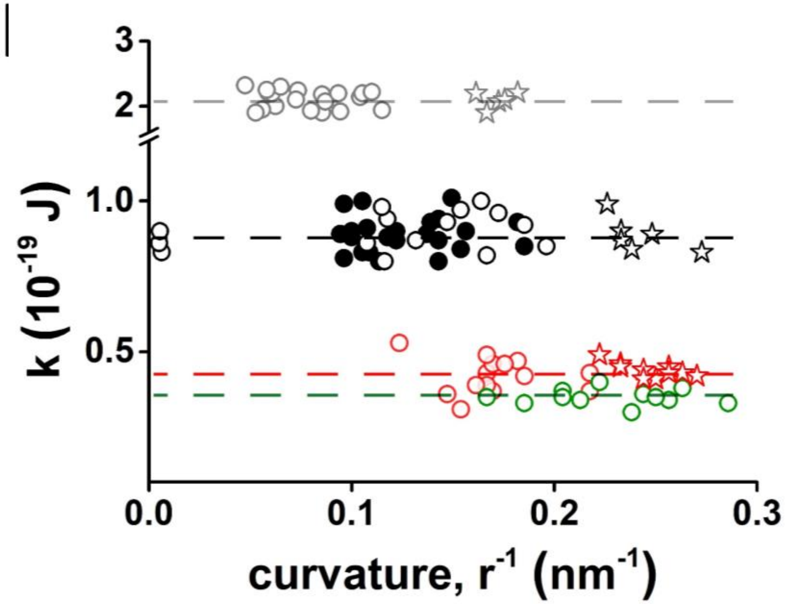


We discriminated three different outcomes of membrane failure to bending stress accumulated in NT pre-fission state: leakless fission, pores formation preceding fission; membrane rupture.

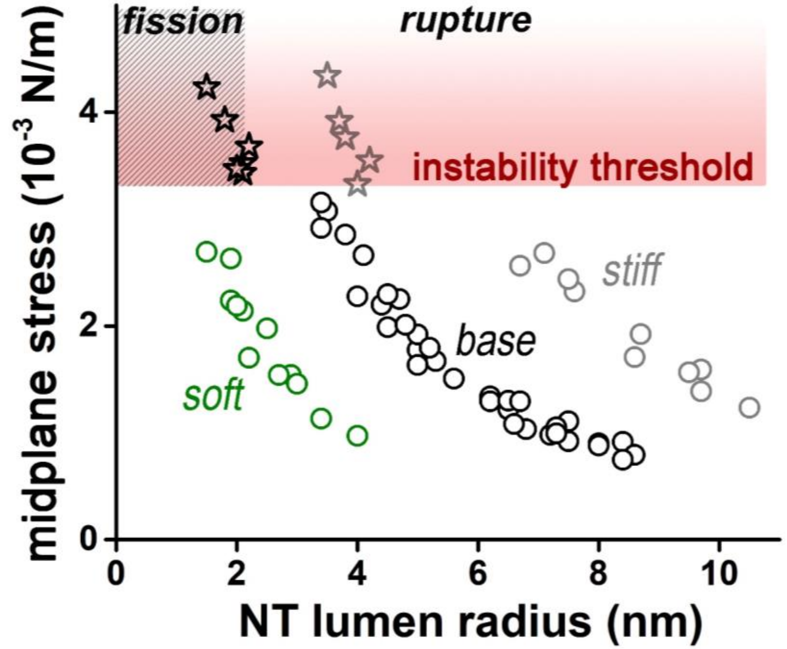
Measurement of membrane bending rigidity at high and low membrane curvatures by applying nanoscale electro-actuation on NT



Voltage ramp induces a change of normalized conductance of NT constricted by CF (upper); linear regression of the dependence of $(r)^{-2}$ on U^2 (lower).

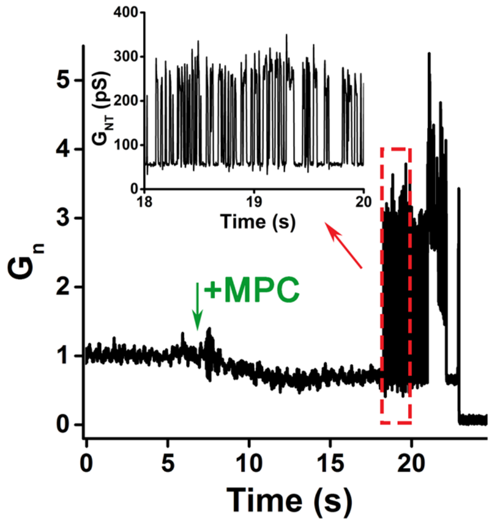


Change of bending modulus, *k* with the curvature of NT membrane, r^{-1} measured for POPC:Chol 1:1 (grey), DOPC:Chol 8:2 (black solid), DOPC:Chol 7:3 (black open), OPC:DOPE 1:1 (green) and DOPC:Chol 7:3 in the presence of ENTH (red)

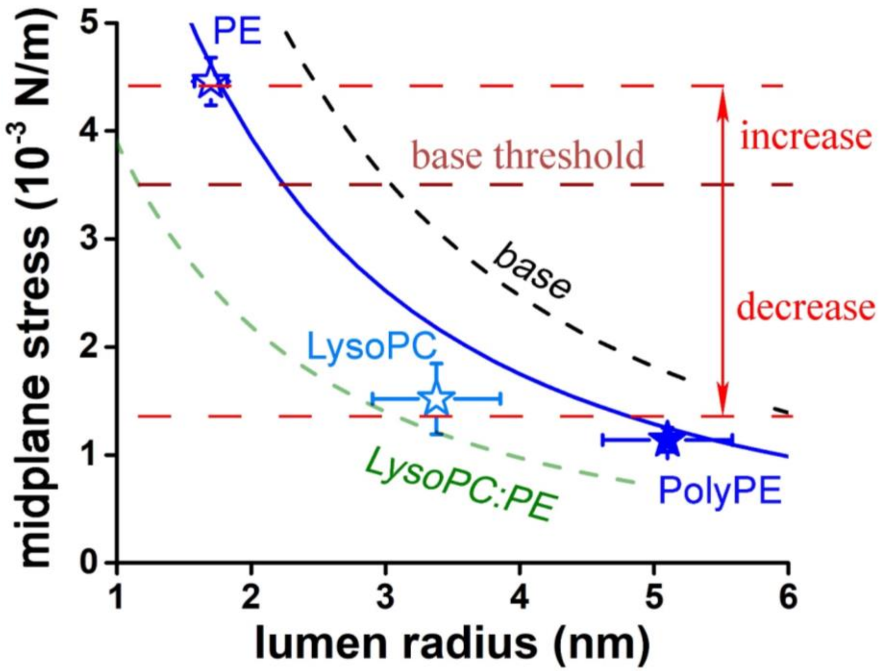


Dependence of NT membrane midplane elastic stress on the NT lumen radius measured for the base (black), stiff (gray), and soft (green) membranes. Fill area indicates elastic stresses lying above the instability threshold at which stochastically structural reorganization of lipid bilayer occurs. Shading marks a region in the stress-radius phase space in which the local loss of structural stability of NT's lipid bilayer does not lead to membrane rupture but is resolved by NT membrane fission.

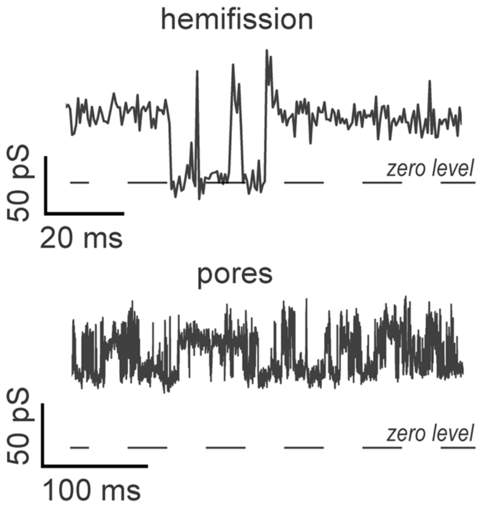
Molecular geometry (spontaneous curvature) of lipids determines the pathway of NT membrane remodeling during its fission



Under similar stress, the presence of conical lipids, such as LysoPC, greatly affects the instability development. MPC induced NT conductnace reduction followed by pores formation in the NT membrane and the NT fission.)



Averaged midplane stress and lumen radius at which structural instability of NT membrane occurs measured for membrane containing LysoPC, DOPE, PolyPE. Curves represent theoretically predicted dependences of midplane stress on lumen radius for the base composition (black), 30 mol% PE or 30 mol% PolyPE containing membrane (blue) and OPC:DOPE 1:1 mixture (olive). Horizontal dashed lines represent the base instability threshold change induced by DOPE (increase) or PolyPE, and LysoPC (decrease).



Both, poration and hemi-fission are reversible at the initial stage of instability, reflected in the cyclic opening/closure of the conductance pathway through the NT (flicker) or its walls (poration)

Conclusion

- Nanoscale deformations of highly curved lipid NT can be described in terms of continuum microscopic elasticity with embedded elastic moduli. In 1D constriction, the description is valid till the point of instability, rendering the latter defect-driven. We identify different pathways the defects take to develop (via nucleation of pore or stalk-type leakless connection) and revealed how the choice is regulated by membrane mechanics and composition.