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Mechanical traits of isolated nuclei inspected via force spectroscopy

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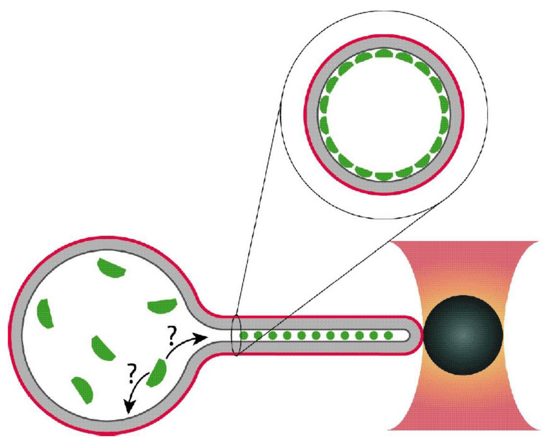
What?

Optically-trapped beads can be used to induce a variety of mechanical stresses upon the membrane of isolated cell nuclei

The magnitude and nature of the perturbation can be used to assess traits such as the elastic properties of the probed nucleus type. Moreover, correlations between the stress and the triggering/disruption of processes coordinated by the nucleus may be stablished

Changes in the optical forces acting upon the probing bead can be directly related to the response of the nuclei, thus revealing target traits

Moreover, simultaneous confocal imaging can expand the picture of the implications of these mechanical perturbations by enabling direct visualization of cellular components involved in the reaction to the stress



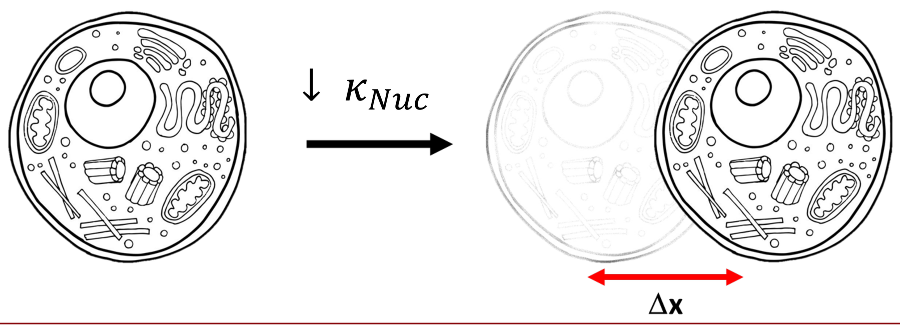
Why?

Cell nuclei are constantly exposed to mechanical forces that trigger dynamic changes in their structure and morphology

Perturbations can imply short-term and long-lasting consequences on the nuclear and the cellular function. The nature of these responses is tied to the force acting upon the nucleus

Mechanical stimuli may alter the nuclear shape, the expression of genes or the organization of the chromatin. While still to be completely understood, responses seem to depend on factors such as direction, intensity and frequency of the stimulus

Altered traits featured by nuclei in cancerous cells are responsible for some characteristics of these cells. One of such is a general decrease of the stiffness of the nuclear envelope which facilitates cell motility and migration



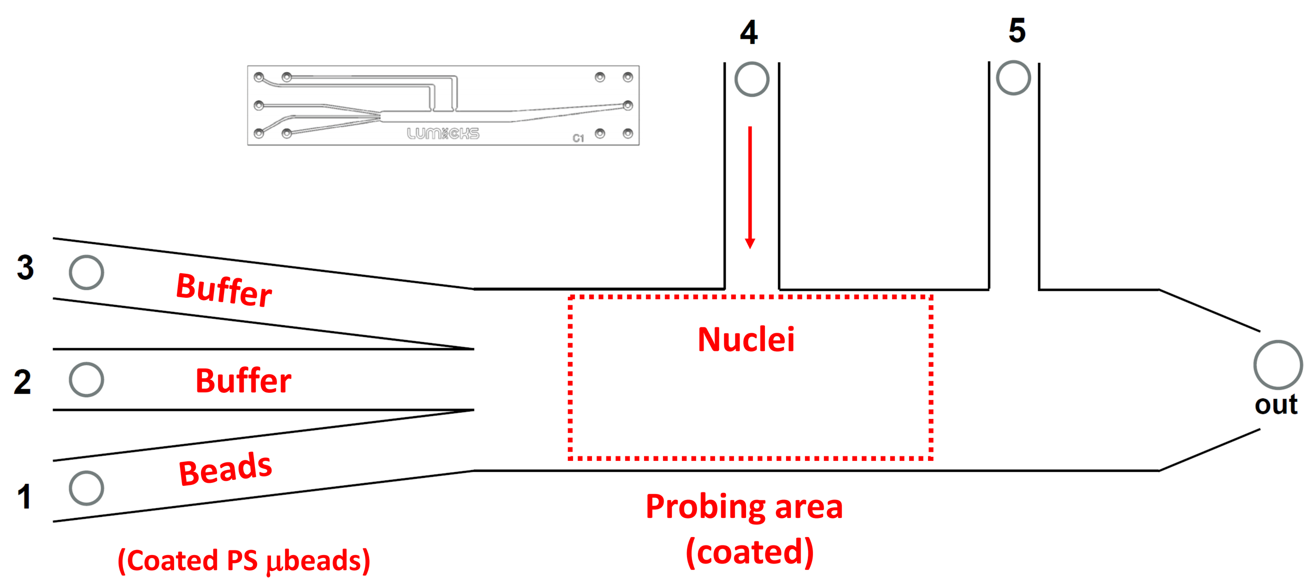
How?

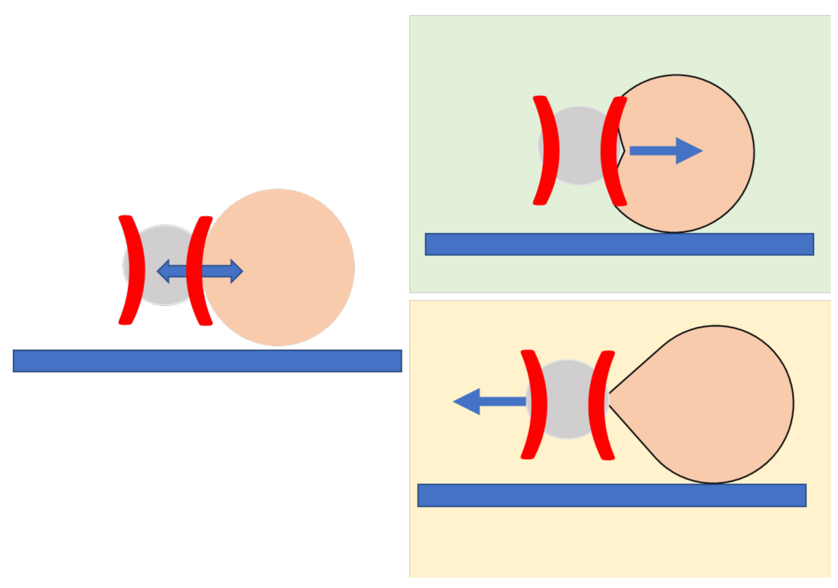
Isolated cell nuclei with marked nuclear pore complexes or lamina are flushed into a coated microfluidic chamber and become attached to the glass bottom before being probed

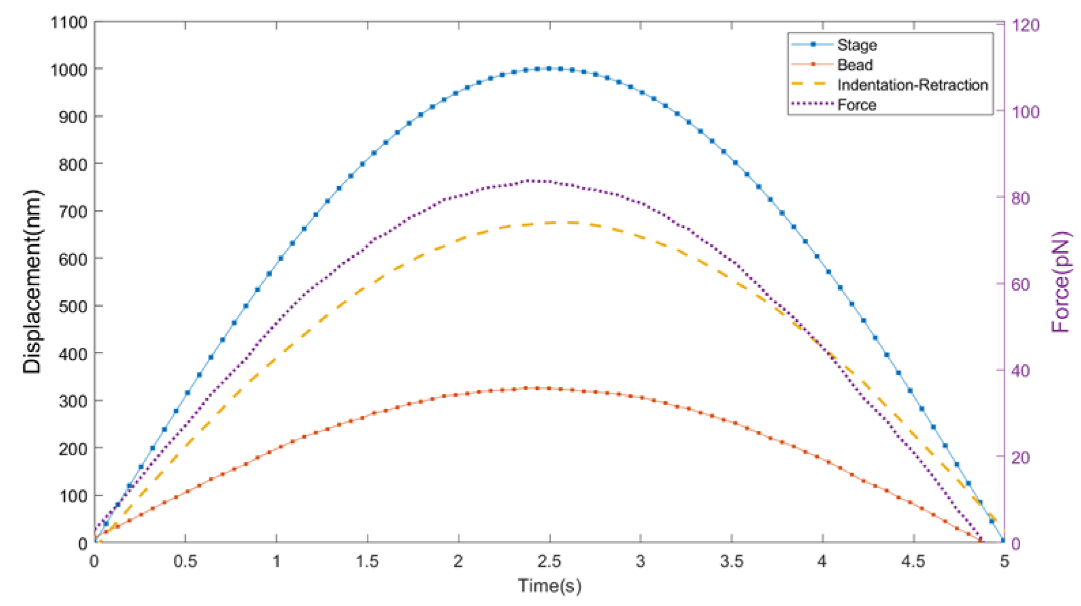
Optically-trapped microbeads coated with streptavidin are used to perform oscillations upon the nuclear envelope. The indentation depth and retraction length as a function of the laser power used to create the optical trap as well as the frequency at which the deformation is induced are tracked via confocal microscopy and changes in the trapping force

From the recorded force/indentation depth ratios, the nuclear stiffness, i.e., the Young's Modulus, can be quantified using the expression: $E = \frac{3(1-\nu^2)}{4\sqrt{I_d R}}\,\mathbf{F/Id}$

The experimental setup used herein (C-Trap, LUMICKS, The Netherlands) allows the use of up to four simultaneous optical traps to perform more complex mechanical stimuli under tightly controlled conditions

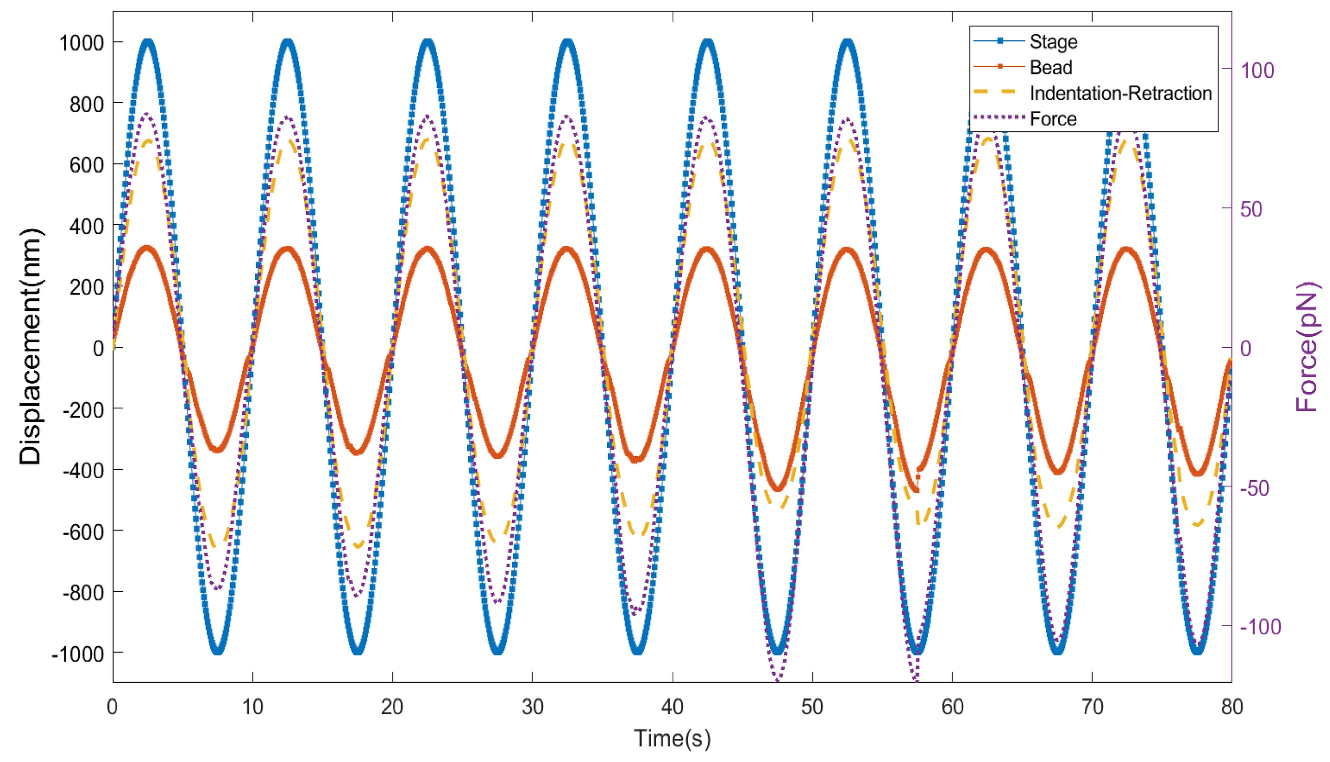


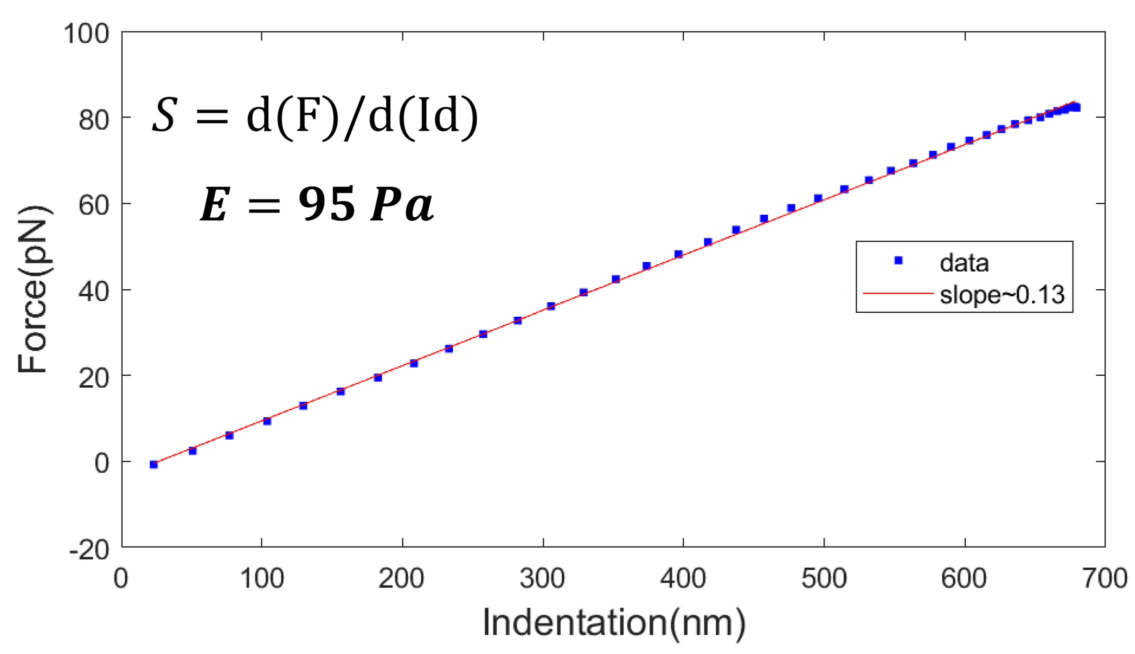


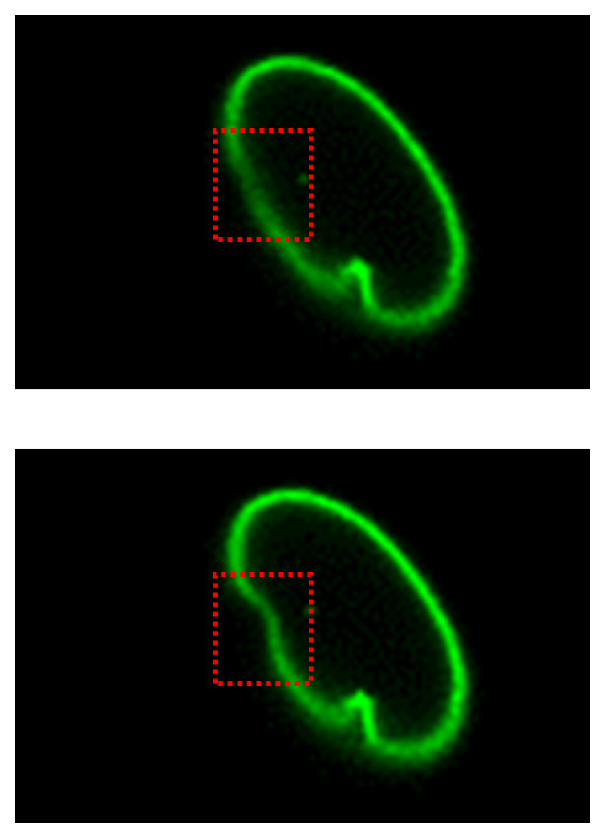


Sounds good, any results?

Nuclear response to oscillations at low frequency (stimuli acting over a long time scale)





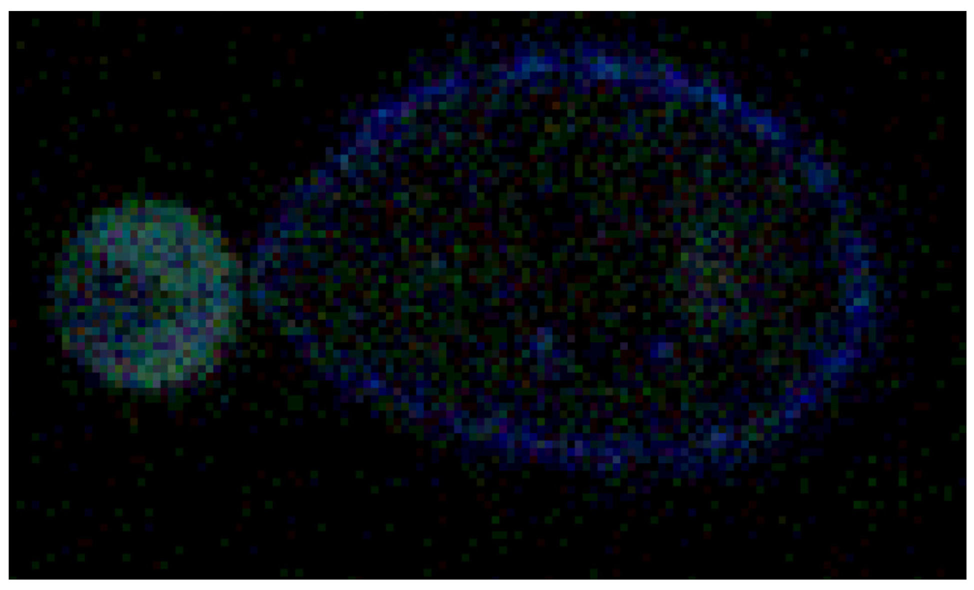


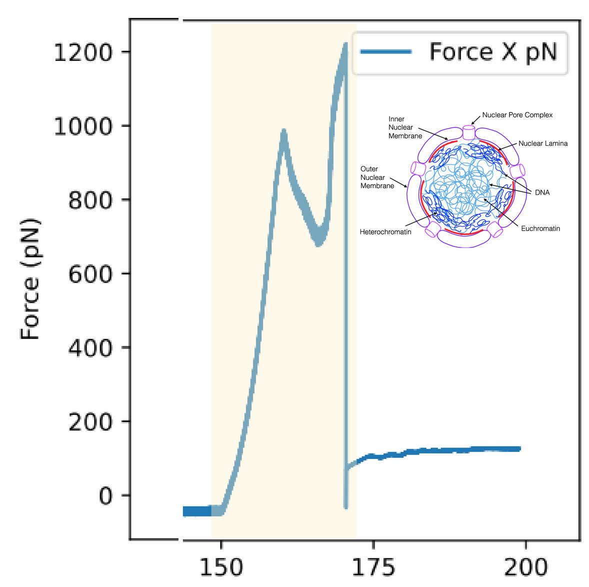
Merging the sensitivity of OT with high magnitude stimuli

Beads trapped at high powers can be pressed into the nuclear envelope to create an intimate interaction

Upon retraction of the bead, nuclei deform to a maximum length before elastically returning to their original shape and pulling the bead out of the trap

During this motion, force curves seem to indicate different behaviors between the inner and the outer layer of the envelope, further experiments will aim to prove this hypothesis





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