CYTOPLASM STIFFNESS CAN REVERSE NUCLEAR PLASTICITY IN LAMIN-DEFICIENT CELLS

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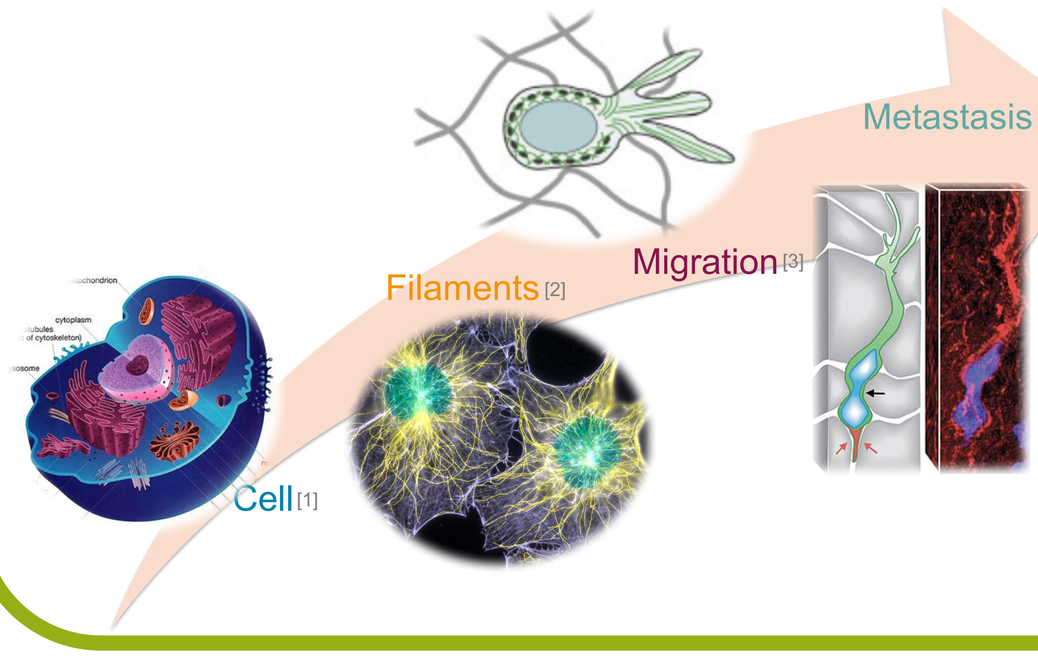
1. FRAMEWORK



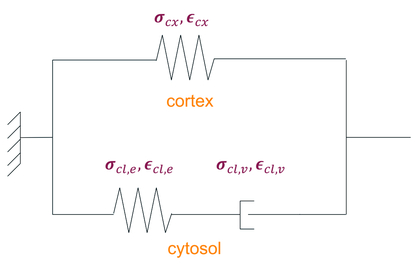
The ability of cells to migrate is a foundation of life, but also of cancer metastasis…

The **nucleus** being the **stiffest** and largest organelle in the cell, it is a regulator of its migratory behaviour.
Moreover, **nuclear plasticity** has been observed [5], potentially facilitating the passage through constrictions once the first one is overcome.

Necessity to study more precisely **nuclear mechanics** and its **interplay with the cytoplasm**

2. RHEOLOGICAL MODELS

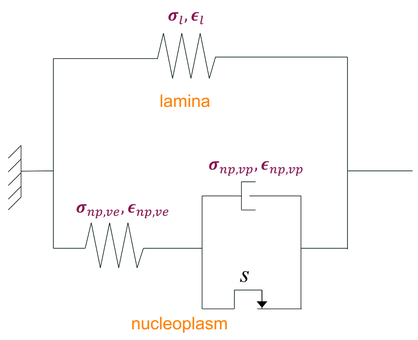
Cytoplasm



$$\sigma_{cytoplasm} = \sigma_{cx} = \sigma_{cl}$$

$$\epsilon_{cytoplasm} = \epsilon_{cx} + \epsilon_{cl}$$

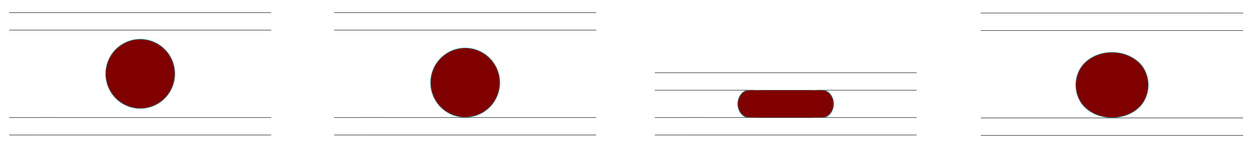
Nucleus

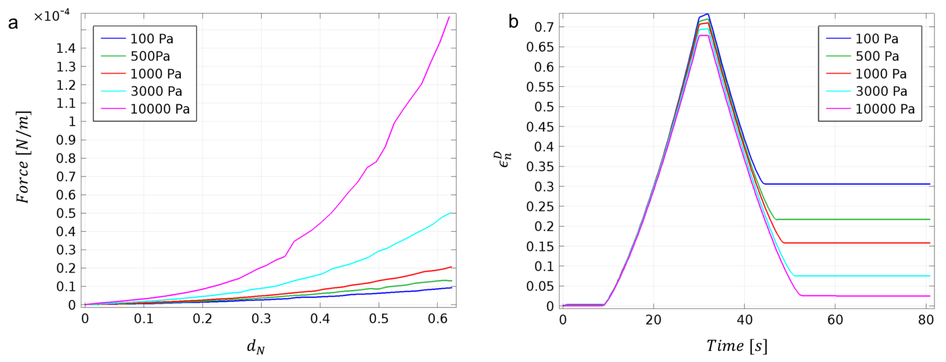


$$\sigma_{nucleus} = \sigma_l = \sigma_{np}$$

$$\epsilon_{nucleus} = \epsilon_l + \epsilon_{np}$$

3. RESULTS : COMPRESSION TEST



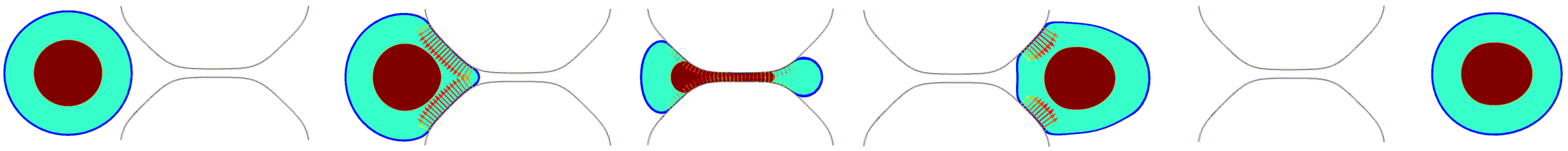


(a) Force-Normalized displacement curve and (b) evolution of the nuclear deviatoric strain with respect to time for various values of lamina's Young Modulus

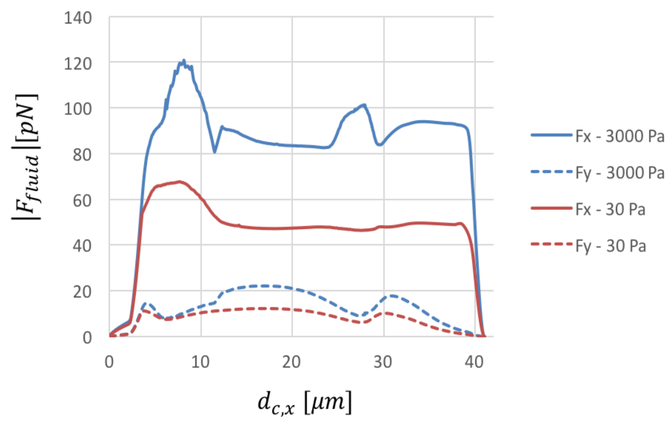
The force-deformation curve is coherent with experimental literature

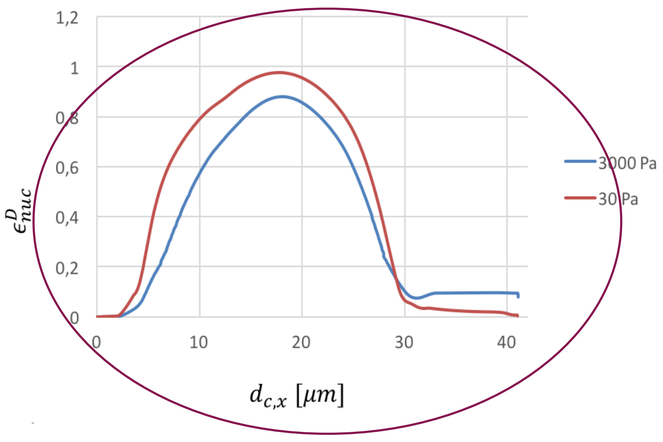
A stiff lamina protects the nucleus from extensive plastic deformation

3. RESULTS : PERFUSION TEST



The cell passively flows through a 1µm-wide micro-constriction under the action of a fluid flow





Comparison of the perfusion test results in the 1 µm-wide micro-channel for wild type and lamin deficient cells.
Left: Resulting fluid force (vertical and horizontal components), Right: Nucleus deviatoric strain

The cytoplasm "pulls" on the softened nucleus and reverses the plastic deformation

Significant mechanical interplay between the nucleus and the cytoplasm

[1] Teresa Audesirk & Audesirk, Gerald. *Biology life on earth* (5th ed) (1999). Upper Saddle River, N.J Prentice Hall
[2] 1st Place in 2003 Nikon Photomicrography Competition, Dr. Torsten Wittmann
[3] Lämmermann, Tim, and Michael Sixt. "Mechanical Modes of 'Amoeboid' Cell Migration." *Current Opinion in Cell Biology* 21.5 (2009): 636–644. *NCBI PubMed*. Web.
[4] Columbia University Medical Center (2009)
[5] Pajerowski, J. David et al. "Physical Plasticity of the Nucleus in Stem Cell Differentiation." *Proceedings of the National Academy of Sciences of the United States of America* 104.40 (2007): 15619–15624. PubMed Central. Web.