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MECHANOBIOLOGY & SOFT MATTER *group*

SPATIAL COORDINATION BETWEEN CELL AND NUCLEAR SHAPE WITHIN MICROPATTERNED ENDOTHELIAL CELLS

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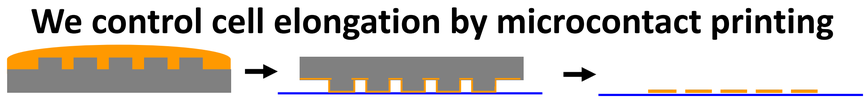
Cell shape changes are involved in many physiological processes such as crawling, spreading, … and are commonly associated with nuclear shape remodeling. In this work, we investigated the mechanism of nucleus regulation by cell shape. To achieve this, we shape-engineered single endothelial cells to quantitatively and non-invasively assess the nuclear morphology and the intracellular force balance in response to cell shape changes. We demonstrate that nuclear deformation in response to cell elongation results from the action of an increased tension in lateral actomyosin filaments. The large nuclear deformations induced by cell elongation lead to a decrease of nuclear volume and an increase in DNA compaction. This intranuclear reorganization induce an alteration of cell proliferation.

We control cell elongation by microcontact printing

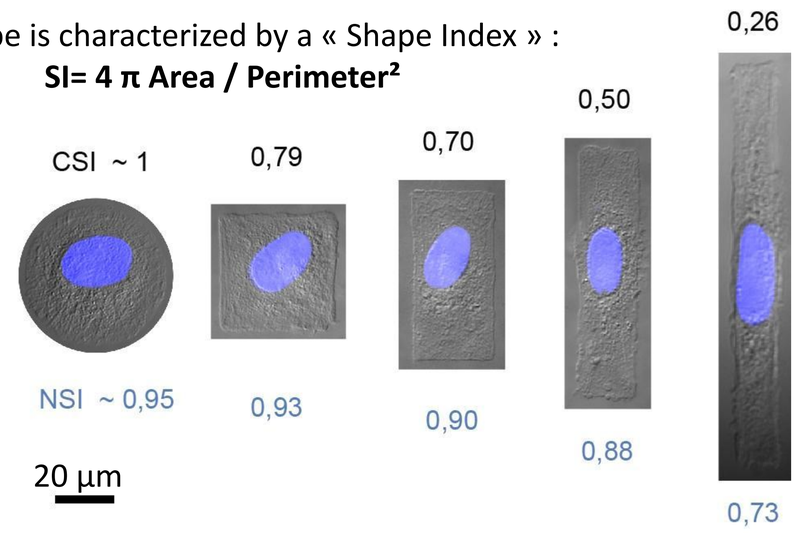


Stamp incubated with fibronectin → Regular distribition of adhesive patterns

Cells grown on these adhesive patterns adopt the shape of the pattern.

The shape is characterized by a « Shape Index » :

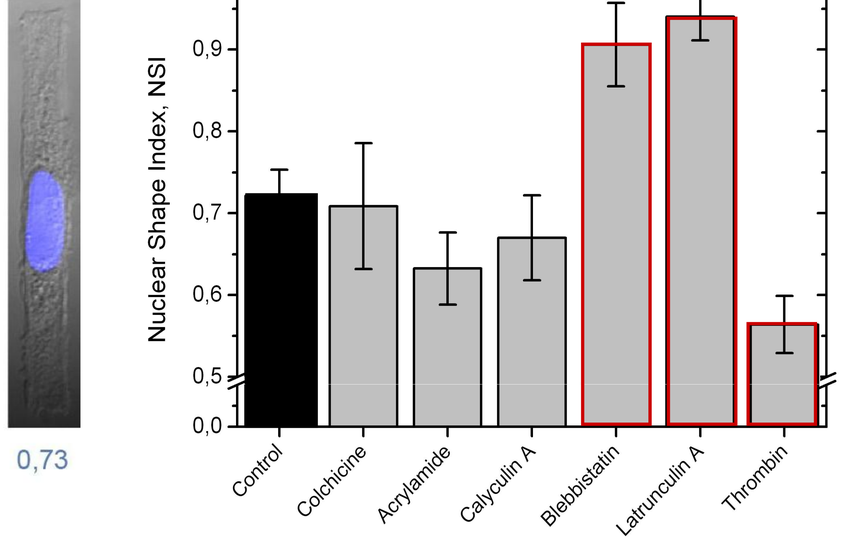
SI= 4 π Area / Perimeter²



Cell elongation induces nuclear deformation

Which component of the cytoskeleton deforms the nucleus?

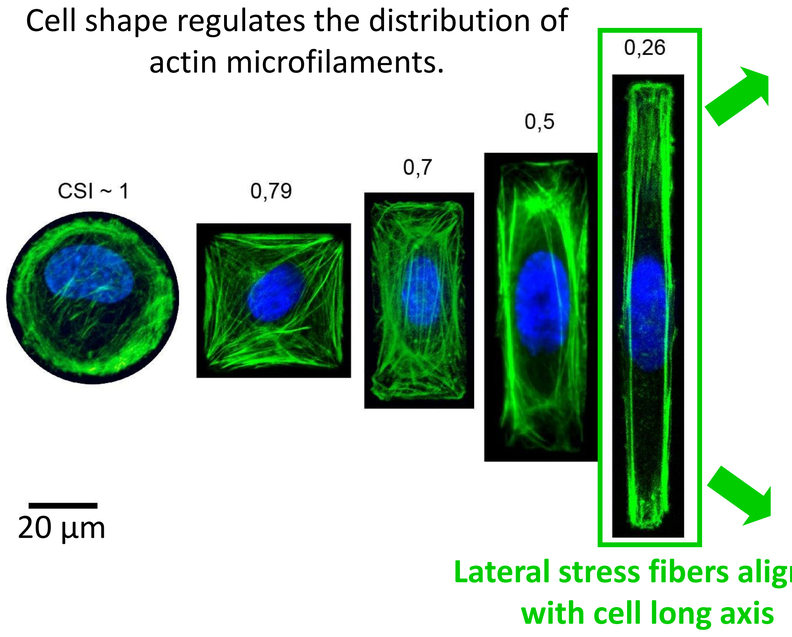
Highly elongated cells (CSI~0,26) were treated with drugs to alter each component of the cytoskeleton or actomyosic contractility, in order to assess their role in the regulation of nuclear shape.



Actin stress fibers and contractility regulate nuclear shape

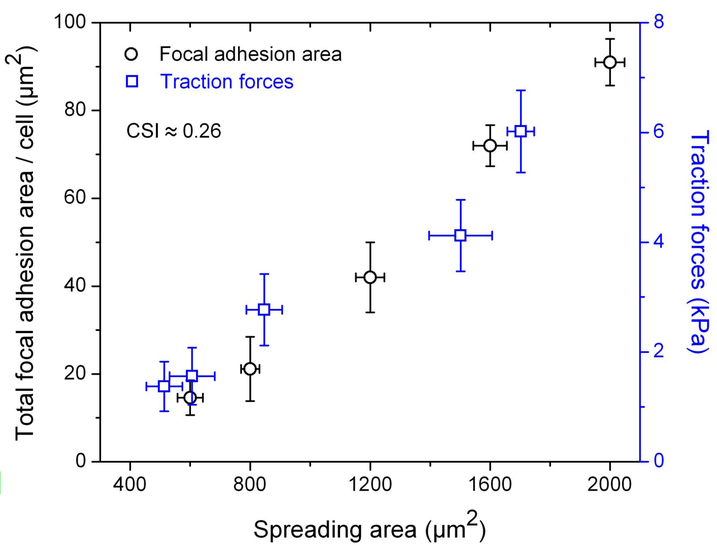
How does the actin cytoskeleton act on the nucleus?

Cell shape regulates the distribution of actin microfilaments.

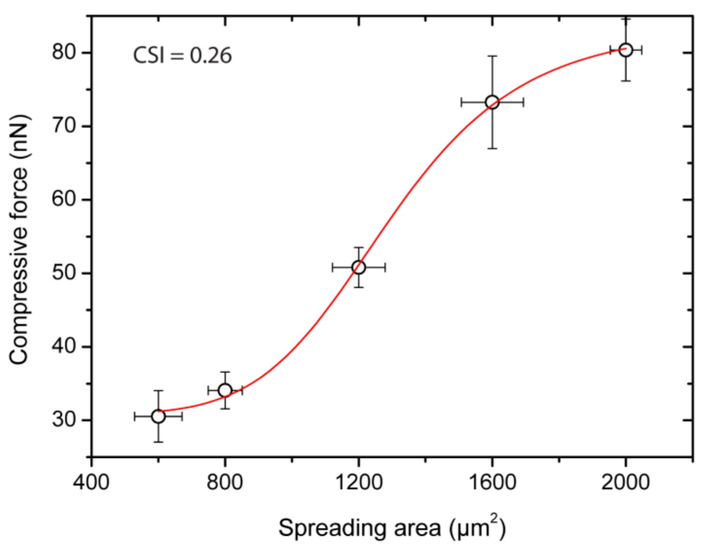


Lateral stress fibers aligned with cell long axis

By traction force microscopy, we measured the forces that **elongated cells** exert on their substrate.



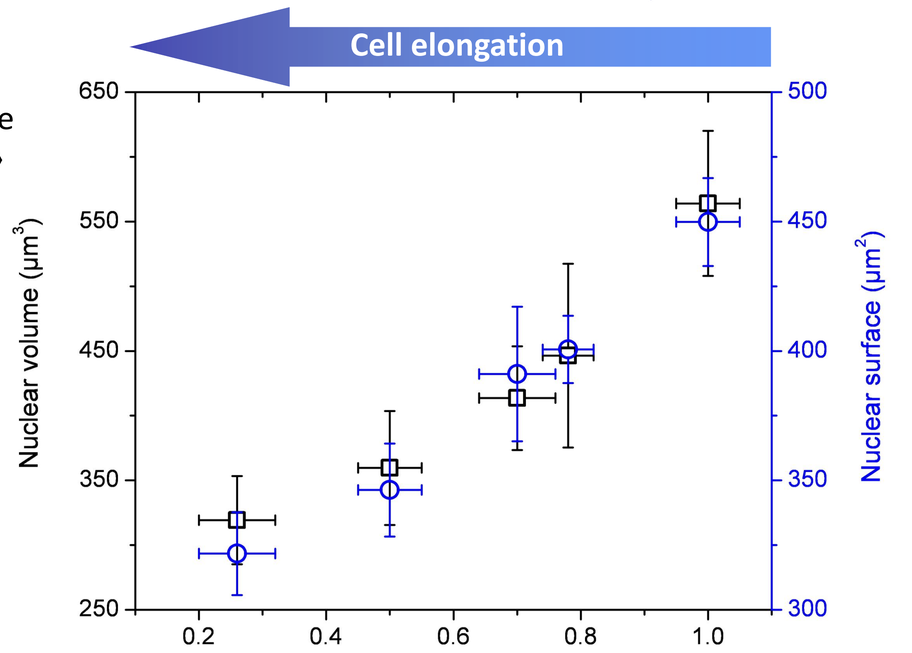
This force is distributed in the lateral stress fibers and allow them to laterally compress the nucleus.



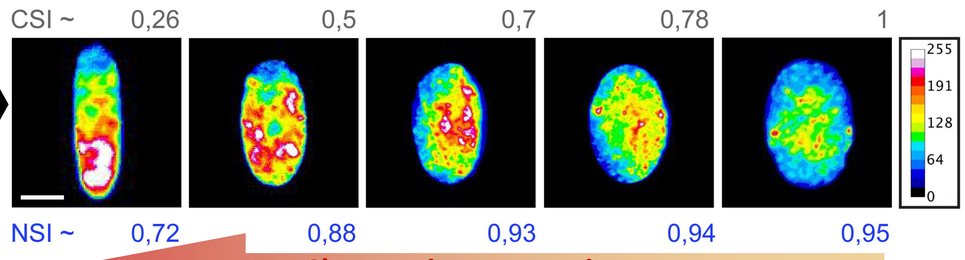
During cell elongation, the nucleus is laterally compressed by tensed actin stress fibers.

What are the consequences of these deformations?

Determination of nuclear volume from confocal 3D images.



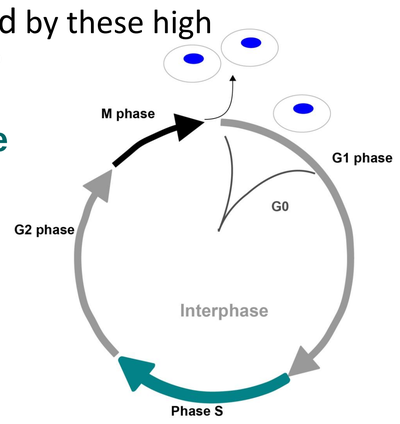
Chromatin compaction maps by mean of DAPI fluorescence intensities.

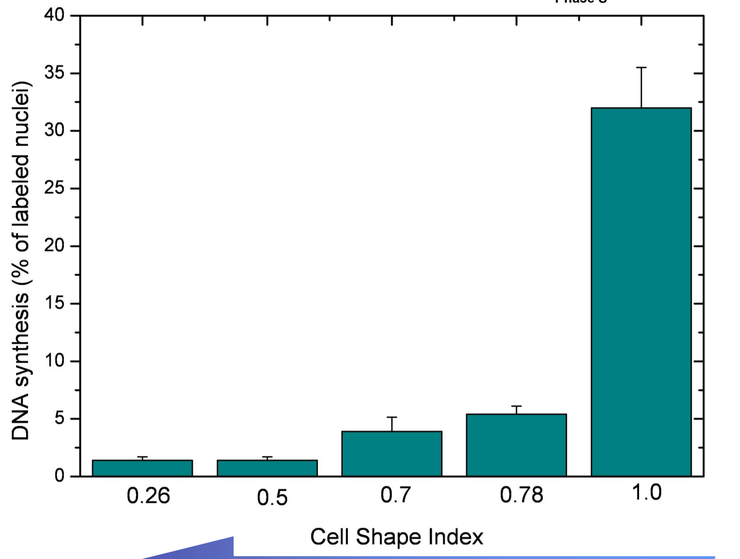


Cell elongation leads to a high **decrease of nuclear volume** and an intranuclear reorganization. Indeed, **DNA compaction** increases during cell elongation.

Is the ability of cells to proliferate altered by these high strains applied to nuclei ?

We added **5-bromo-2-deoxyuridine** to shape-engineered cells to label cells that are replicating DNA, during the **S phase** of the division cycle.





Conclusion:

- Cell regulates the shape of its nucleus thanks to the **actin cytoskeleton** and **actomyosic contractility**.
- During cell elongation, stress fibers formed on each side of the nucleus **laterally compress the nucleus** and deform it.
- In addition to shape changes, stress fibers compression of the nucleus induce a **large loss of nuclear volume** and a **compaction of DNA**.
- As a result of these nuclear alterations, the **ability of elongated cells to replicate DNA and to divide is strongly decreased**.

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