Deformation-induced chromatin condensation in the cell nucleus

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Eukaryotic cells in tissues are constantly subjected to several mechanical stimuli acting over different scales. For instance, shear stresses due to fluid flow, cell contractility, substrate stiffness, and cell migration all contribute to generating mechanical cues, which are then transmitted to the cell nucleus. Inside the nucleus, the DNA is stored by wrapping around proteins called histones in a “beads on a string” structure, the chromatin, which permeates the nucleus during most cell phases. Chromatin can be thought of as a polymer gel that is spatially organized into two coexisting phases: less packed and genetically-active regions called euchromatin and tightly packed and genetically-silent regions called heterochromatin (see Figure 1(a-b)).

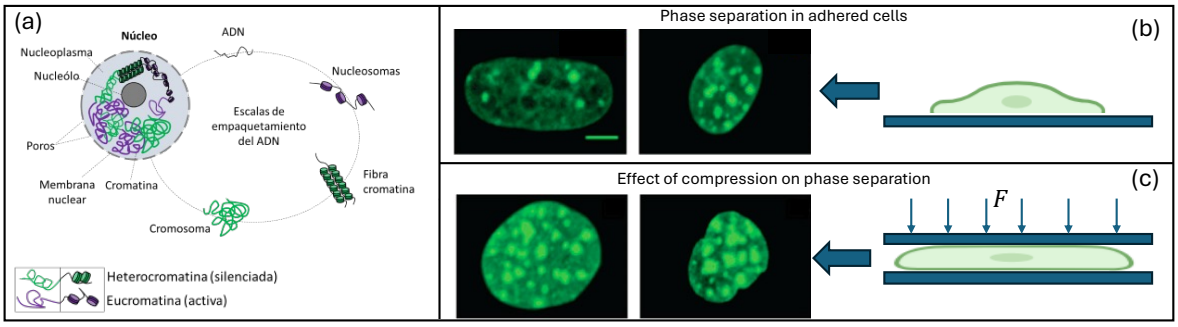

Figure 1: (a) Schematic description of the chromatin organization inside the nucleus. (b) Fluorescent image of a cell nucleus where the regions of heterochromatin display larger fluorescence intensity. (c) Compression of the nucleus condenses chromatin and increases the amount of heterochromatin.

Experimental observations show that nuclear deformations can alter the balance between euchromatin and heterochromatin regions, promoting condensation of chromatin through the formation of more heterochromatic regions (see Figure 1(b-c)). Such reorganization of chromatin results in a change in the genetic information expression, potentially leading to cell reprogramming into tumor precursors, fracture of the nucleus, and DNA damage, all of which are detrimental to the organism's health. Many questions remain open regarding the deformation-induced chromatin condensation: Is it reversible upon the release of deformation? Does it depend on the type of deformation applied to the nucleus? What is the underlying physical mechanism?
In this talk, I show our efforts in addressing these questions by in vitro and in silico analysis. We employ confined cell migration experiments combined with fluorescent microscopy to visualize the changes in chromatin condensation regions as the cell migrates through microfluidic constrictions. We then try to rationalize our experimental results and those previously obtained in the literature using a model based on a chemically-active polymer gel theory. Our findings shed light on how mechanical stimuli are translated into changes to genetic information transcription, which has implications for the development and progress of pathologies.