Revealing label-free, multiplexed molecular information for mechanobiology through Raman spectroscopy and advanced data science

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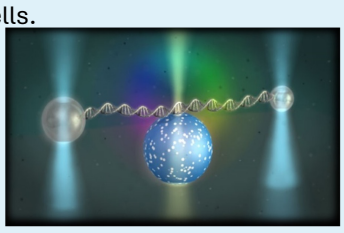
Methods capable of simultaneously revealing the molecular response of cells to mechanical perturbation without exogenous labels remain scarce. Raman spectroscopy (RS) provides highly specific molecular information of living cells and tissues in a label-free and multiplex way. We envision that the combination of RS with advanced chemometric and data science approaches can bridge this gap. Here, we present the evolution of a research line aimed at establishing RS as a label-free and multiplexed molecular readout for mechanobiology

We combined **RS and optical tweezers to simultaneously manipulate and probe biological samples**, demonstrating the feasibility of monitoring force-induced molecular changes in DNA molecules and red blood cells.



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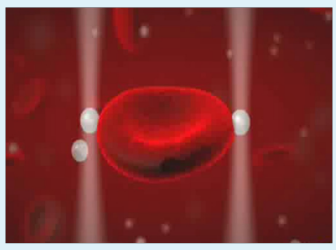

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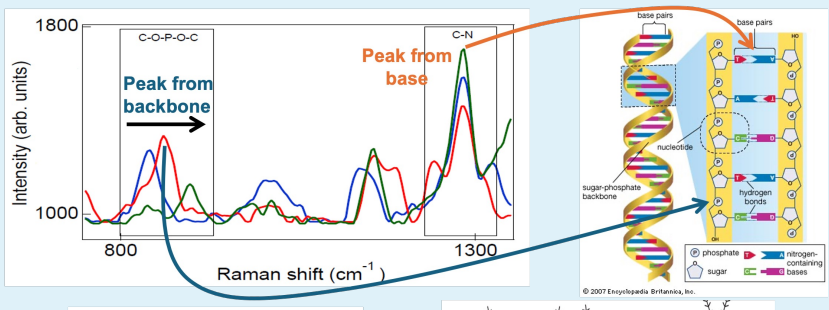
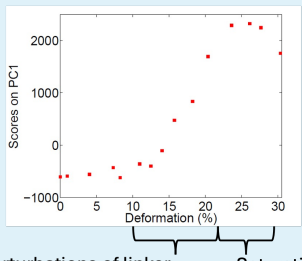
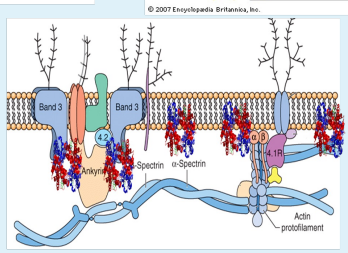


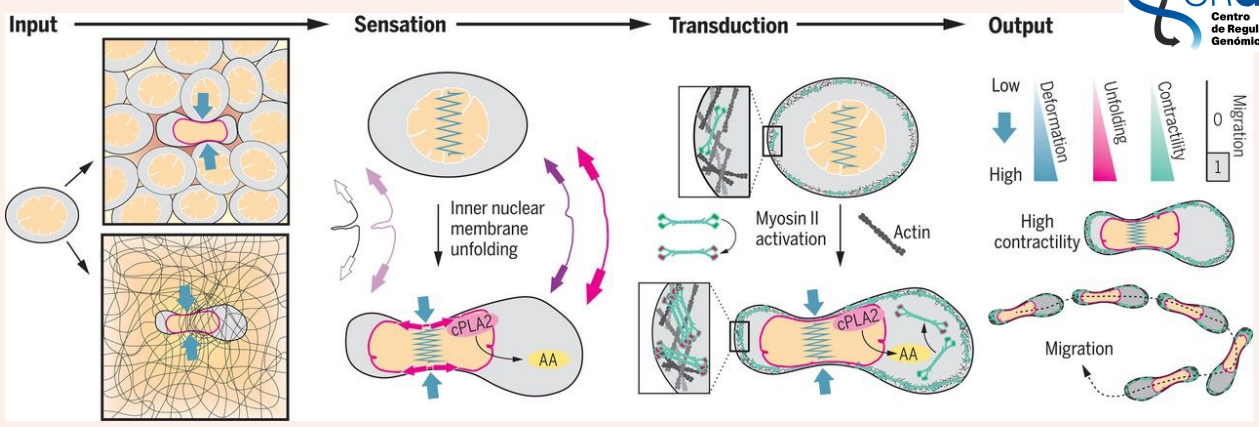


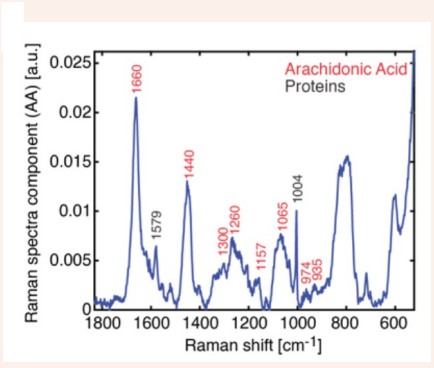


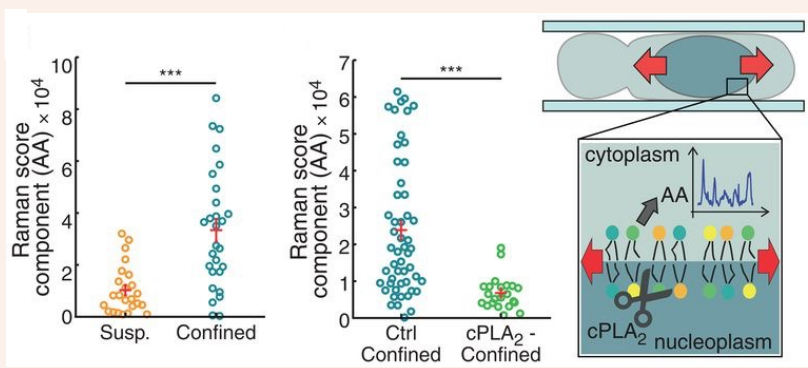
Structural perturbations of linker proteins, spectrin network and hemoglobin occur

Saturation of signal with stretching shows mechanical nonlinearity

We applied this approach to investigate the **molecular response of living cells under mechanical confinement**, revealing that cPLA2 activity at the inner nuclear membrane produces arachidonic acid, which is a metabolite regulating cortical contractility in confinement (in collaboration with V. Ruprecht, S. Wieser and V. Venturini). Importantly, these findings demonstrated that **label-free RScan identify biochemical pathways activated by mechanical stress in living cells combined with advanced data science.**

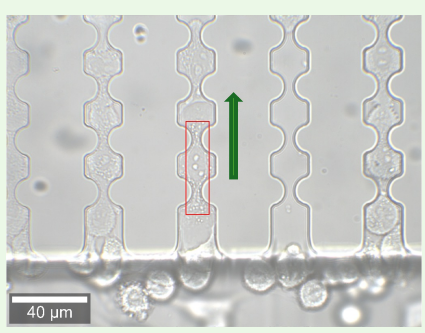


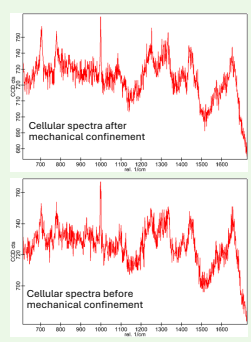




V. Venturini, et al **Science**, 370, eaba2644, 2020

We are currently extending this framework to **cancer mechanobiology** by developing label-free Raman imaging strategies to study **cancer cells migrating through highly confined microfluidic channels and cancer organoids** (collaboration with MJ Gomez and JM Garcia-Aznar from M2BE group). By integrating molecular imaging with advanced computational analysis, we aim to uncover molecular programs associated with confinement, invasion and mechano-transduction in physiologically relevant models.





These studies lay the foundations for a **next-generation mechanobiology platform that integrates mechanical perturbation, label-free RS and advanced data science methods** to decode mechano-transduction across biological systems, from single biomolecules to cancer organoids.

Ayuda CEX2023-001286-S financiada por