Investigation of cell mechanics using Nanodevices and Nano-instruments: some examples

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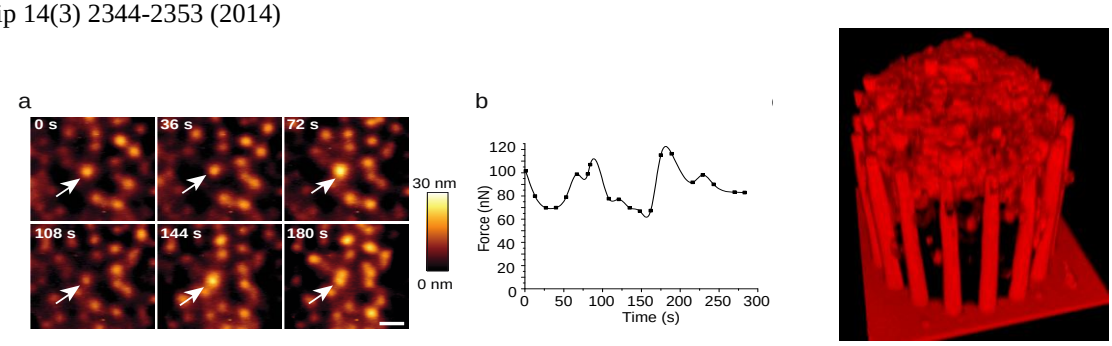
It is now well established that to perform their various functions, cells undergo a large range of intra and extracellular events, which involve mechanical phenomena at both the micro and nanoscale. Cells are able to sense forces and stiffness (mechanosensing) and to transduce them into a cascade of biochemical signals leading to a context specific cell response (mechanotransduction). At the core of the mechanical activity of cells are the components of their cytoskeleton acting as contractile cables actuated by proteic nanomotors. The nanoscale is thus the appropriate one for investigating the organisation of the active mechanical components and also for the measurement of the exerted forces at a subcellular level . On the other hand the microscale is adapted for upscaling these investigations to cell aggregates and tissues. The nanomechanics of cells is today a flourishing domain of activity in which new methods derived from micro/nanotechnologies have been developed for shedding some light and quantitative values in the mechanosensing properties of cells. This fundamental activity in cell biology meets some medical perspectives as mechanical properties of cancer cells and tumours turned out to differ significantly from normal cells or tissues.
After a short presentation of the biological knowledge related to cell mechanics, I will present some elegant methods coming form the micro/nano community that starts to become standard methods. In particular at the nanoscale, the use of Atomic Force Microscopy (AFM) to sense the rigidity of cells (1) or to measure the force exerted by living cells (2) will be exemplified through the investigation of human macrophages. At the microscale, I will show how the forces generated by adherent cells can be investigated using flexible micrometric pillars of polydimethylsiloxane (PDMS) and how this method can be upscaled to measure the forces generated by growing aggregates of cells in the context of tumor growth and metastasis nucleation (3).

(1) Dynamics of podosome stiffness revealed by atomic force microscopy, A. Labernadie, C. Thibault, C. Vieu, I. Maridonneau-Parini, GM Charrière, Proceedings of the National Academic of Sciences 107 (49), 21016-21021 (2010)
(2) Protusion force Microscopy reveals oscillatory force generation and mechanosensing activity of human macrophage podosomes, A. Labernadie, A. Bouissou, P. Delobelle, S. Balor, R. Voituriez, A. Proag, I ; Fourquaux, C. Thibault, C. Vieu, R. Poincloux, GM Charrière and I. Maridonneau-Parini, Nat. Comm. (5) 2014
(3) Microdevice arrays of high aspect ratio polydimethylsiloxane pillars for the investigation of multicellular tumour spheroid mechanical properties, L. Aoun, P. Weiss, B ; Ducommun, V. Lobjois and C. Vieu, Lab on Chip 14(3) 2344-2353 (2014)



a,b) AFM images of the adhesive structures of living human macrophages (podosomes) and extraction of the quantitative measurment of the time oscillating force of an individual podosome. c) A Micro-device of high aspect ratio PDMS pillars for sensing the force of a growing tumoral spheroid.