Mechanical Assessment of Living Cells

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Cell mechanical properties provide an integrated view of many biological phenomena including cytoskeleton organization, adhesion strength, cellular prestress. These phenomena play a key role in many cellular functions including cell shape, polarity locomotion, proliferation, growth, gene expression, differentiation, mechanotransduction, enzyme anchorage. Changes in cell mechanical property may also reflect cellular adaptation to extracellular environment in response to active external forces or to passive mechanical properties of the extracellular environment notably stiffness of tissue where cells are embedded. The close link existing between cell mechanical properties, cell structure and cell function is realized by the cytoskeleton which is composed of actin filament, microtubules, intermediate filament and associated intracellular and transmembrane cross-linking proteins. Depending on their arrangement, on cell type and extracellular conditions, cytoskeleton elements alternatively behave as passive or active cell sensitive elements, allowing the cell to respond and adapt to changes in biochemical or biomechanical conditions. Thus, measuring cell mechanical properties in relation with cell structure is a crucial step to understand fundamental biological processes. To deduce mechanical properties of living cells, constitutive stress-strain relationships need to be measured over short periods of time (e.g., of the order of a minute) and rheological/mechanical/mathematical models need to be used. Advantageously, the short term mechanical response may also be used to reflect the cellular response at the longer term, i.e., reflecting the effect of changing biological/mechanical extracellular conditions.

Atomic Force Microscopy provides a unique tool to assess the mechanical and structural properties of living cells in controlled environments. We have estimated the local cellular stiffness in a variety of living cells using an AFM NanoWizard®. Using optical calibrated images provided by the Direct Overlay® system and a semi-automatic analysis performed by a homemade Graphical User Interface (GUI) written in Matlab®, we were able, in a chosen zone of the living cell, to calculate a stiffness map and superimpose the results to the optical image of the cell (fluorescence or transmission). The global result is an interactive visualization of the map of calculated Young Modulus that can be associated with the visualization of the measurement position on the optical image calibration. The GUI can also integrate various mechanical models notably to take into account the shape of tip cantilever and/or more complex force-indentation law.

We will show how mechanical data provided with this approach correlate with the inner components of the cellular substructure, such as the nucleus, stress fibers or other cytoskeleton filaments, as well the lamellipodium structure during cellular extension. On the whole, this coupled mechanical and structural analysis allows better understanding of various biological and mechanical processes behind cellular functions and behind the interactions between the cell and the extracellular medium.

Bibliography

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