Probing mechanical properties of living cells with AFM

Daniel Navajas
dnavajas@ub.edu
Unitat de Biofisica i Bioenginyeria, School of Medicine
University of Barcelona, 08036 Barcelona, Spain.

Abstract

Mechanical properties of cells play a critical role in many essential biological functions including migration, contraction, differentiation and gene expression. Moreover, cells feel and actively respond to adhesive forces and deformations exerted by the adjacent cells and the extracellular matrix. The cell mechanical behavior is increasingly recognized as a key determinant of the normal cell function and of its alteration under pathological conditions. However, quantitative knowledge of the mechanical behavior of the cell remains largely incomplete. Atomic force microscopy (AFM) allows 3-D manipulation of cells and molecules with nanometric resolution with simultaneous measurement of the applied force with pN sensitivity. These are the displacement and force scales suitable for probing single molecules and cells. Moreover, measurements can be carried out in liquid with controlled environmental conditions and the cell response to pharmacological agents can be monitored in real time. Therefore, AFM is a powerful tool for probing the mechanical behavior of living cells. Nevertheless, accurate measurements require consideration of both the characteristics of the technique and the features of the biological sample. Cell stiffness is probed by indenting the cell surface with the cantilever tip. The force-indentation curve provides an estimation of the apparent Young modulus of the cell. A robust approach for probing cell viscoelasticity is to apply small amplitude sinusoidal oscillations [1,2]. Accurate computation of the cell viscoelastic modulus demands the correction of raw force-indentation oscillatory data for the cantilever viscous drag [3]. Nevertheless, the relative magnitude of the hydrodynamic artifact increases with frequency, which makes it difficult to obtain reliable measurements of the viscoelastic modulus at frequencies higher than a few hundreds of Hz. Computation of cell mechanical modulus requires precise knowledge of the tip geometry and the use of a correct tip-cell contact model. Conventional AFM pyramidal tips can be used for both cell imaging and mechanical measurements [5]. On the other hand, sharper tips used for high resolution imaging have poorly defined geometry and are not well suited to mechanical measurements. Cell adhesive properties are probed by binding a ligand-coated tip to cell membrane receptors and retracting the cantilever until tip detachment. Tip-cell contact models of conventional tips under adhesive conditions are poorly defined. We have recently developed flat-ended cylindrical tips nanofabricated with ion beam technology [6] that provides a well defined and constant tip-cell contact area, which facilitates cell measurements.

References

[1] Alcaraz J, Buscemi L, Grabulosa M, Trepat X, Fabry B, Farré R, Navajas D. Microrheology of human lung epithelial cells measured by atomic force microscopy. *Biophys J* 84: 2071-2079, 2003.

[2] Roca-Cusachs P, Almendros I, Sunyer R, Gavara N, Farré, Navajas D. Rheology of passive and adhesion-activated neutrophils probed by Atomic Force Microscopy. *Biophys J* 91: 3508-3518, 2006.

[3] Alcaraz J, Buscemi L, Puig-de-Morales M, Colchero J, Baró A, Navajas D. Correction of microrheological measurements of soft samples with atomic force microscopy for the hydrodynamic drag on the cantilever. *Langmuir* 18: 716-721, 2002.

[4] Rico F, Roca-Cusachs P, Gavara N, Farre R, Rotger M, Navajas D. Probing mechanical properties of living cells by atomic force microscopy with blunted pyramidal cantilever tips. *Phys Rev Stat Nonlin Soft Matter Phys* 72: 021914, 2005

[5] Roca-Cusachs P, Alcaraz J, Sunyer R, Samitier J, Farré R, Navajas D. Micropatterning of single endothelial cell shape reveals a tight coupling between nuclear volume in G1 and proliferation. *Biophys J in press* (ahead of print doi:10.1529/biophysj.107.116863).

[6] Rico F, Roca-Cusachs P, Sunyer R, Farré R, Navajas D. Cell dynamic adhesion and elastic properties probed with cylindrical atomic force microscopy cantilever tips. *J Mol Recognit* 20: 459–466, 2007.