

Atomic force microscopy cantilevers beyond imaging

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The importance of the characterization of movement in biological samples ranges from the fields of biology and microbiology to pharmaceuticals and drug development. For instance, the movement of living systems can deliver useful information regarding the metabolism of the specimens and can be used to define their response to external stimuli.

Here, I will show how nanomotion sensors can be used to characterize the nano-sized movements of specimens of interest in the fields of biology, microbiology and pharmacology. This sensor exploits the sensitivity of the atomic force microscopy cantilever and combines it with the innate correlation between life and movement. When we induce the adhesion of living systems on cantilevers, their metabolic activity induces fluctuations of these sensors. If the exposure to a particular drug will cause the death or inactivation of the specimens, the fluctuations will be reduced in amplitude and this will indicate, in minutes, the effectiveness of the drug.

I will show how the nanomotion sensor can study the movements of different bacterial species [1, 2], of yeasts and fungi when exposed to various external stimuli. Furthermore I will discuss how the extremely high sensitivity of this system can be applied to study conformational changes in proteins and protein complexes [3].

In the case of the study of bacteria I will show how the fast response of the sensor, which is independent of bacterial replication rate, will have many applications in research and applied fields and in particular on the medical practice, with evident advantages for patients care. For instance, by combining it with protocols to achieve rapid isolation of bacteria from clinical samples, we have obtained a rapid and complete characterization of a bacterial infection directly from a clinical source. [4]

The sensitivity and time resolution of the sensor opens the way to many important applications in many medically relevant fields. For example, we have exploited the nanomotion sensor to characterize of the effect of alfa-synuclein on neurons. This study could have wide impact in the study of neurodegenerative diseases, demonstrating at the single cell level the effect of the different protein aggregation forms. [5]

We have also applied this technique to achieve a rapid, accurate and cost-effective characterization of the response of cancer cells to anti-tumoral drugs, with evident impact in the field of oncology. In fact, just as in the case of the characterization of bacteria, by using the nanomotion detector we can determine the most appropriate therapeutic option for a given cancer in a time-range of hours.

In very general terms, all these pioneering results indicate that there is a close correlation between movement and life and that a sensor capable of transducing these movements can deliver a new point of view in the analysis of living systems and allow a new means to characterize the metabolic activity. This has also led us to propose this nanomotion sensor as an innovative technique to detect life in extreme environments. [6]

These studies define how a nanomotion investigation can be used to characterize biological samples and how this information can be used to understand better their metabolic pathways. The speed and sensitivity of the sensor as well as its versatility, will have a massive impact, with applications in general and molecular biology, microbiology, drug development and medicine.

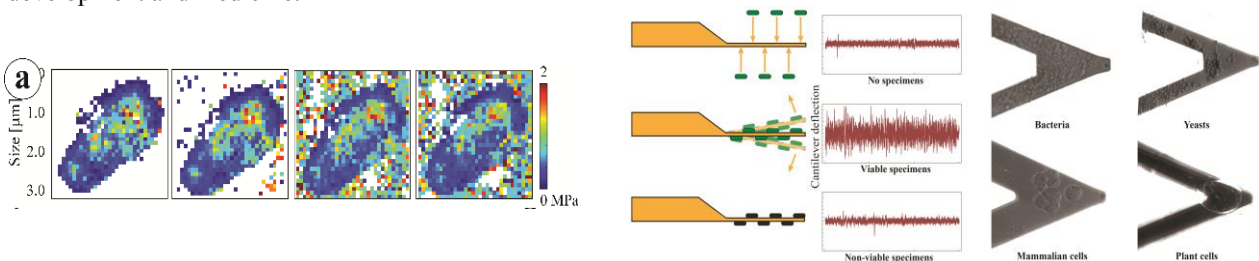


Figure 1. Left panel: AFM nanomechanical analysis of living *E. coli* exposed to ampicillin. In minutes, the cytoplasm can be seen pouring out of the bacteria. Right panel: Schematics of a nanomotion experiment and images of different specimens attached to a sensor.

- [1] Longo et al., Nat. Nanotech., 8, 522-526, (2013)
- [2] Aghayee et al. J. Mol. Rec. 26, 590-595 (2013)
- [3] Alonso-Sarduy et al. PLoS ONE 9, e103674 (2014)
- [4] Longo et al. Clin. Microbiol. Infect., Submitted
- [5] Ruggeri et al. in preparation
- [6] Kasas et al., PNAS, 112 (2), 378–381 (2015).