Breaking Speed and Resolution Limitations of AFM

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High-speed atomic force microscopy (HS-AFM) is a powerful technique that provides dynamic movies of biomolecules at work [1].

To break current temporal limitations to characterize molecular dynamics using HS-AFM, we developed HS-AFM height spectroscopy (HS-AFM-HS), a technique whereby we oscillate the HS-AFM tip at a fixed position and detect the motions of the molecules under the tip. This gives sub-nanometer spatial resolution combined with microseconds temporal resolution of molecular fluctuations. HS-AFM-HS can be used in conjunction with HS-AFM imaging modes, thus giving access to a wide dynamic range [2].

To break current resolution limitations, we developed Localization AFM (LAFM). By applying localization image reconstruction algorithms to peak positions in high-speed AFM and conventional AFM data, we increase the resolution beyond the limits set by the tip radius and reach quasi-atomic resolution on soft protein surfaces in native and dynamic conditions. The LAFM method allows the calculation of high-resolution maps from either images of many molecules or many images of a single molecule acquired over time, opening new avenues for single molecule structural analysis [3].

[1] Ando et al., PNAS, 2001, 98(22):12468-12472, A high-speed atomic force microscope for studying biological macromolecules
[2] Heath et al. Nature Communications, 2018, 9(1):4983, High-Speed AFM Height Spectroscopy (HS-AFM-HS): Microsecond dynamics of unlabeled biomolecules
[3] Heath et al. Nature, in press, Localization Atomic Force Microscopy

Simon Scheuring is Professor of Physiology and Biophysics in Anesthesiology at Weill Cornell Medicine, New York, USA. He is a trained biologist from the Biozentrum at the University of Basel, Switzerland (1992−1996). During his Ph.D. (1997−2001) in the laboratory of Andreas Engel, he learned electron microscopy and atomic force microscopy, and got interested in membrane proteins. During this period, he worked on the structure determination of aquaporins and sugar transporters. During his postdoc (2001−2004) and research assistant (2004−2007) at the institut national de la santé et de la recherche médicale (INSERM) and the Institut Curie in Paris, France, in the laboratory of Jean-Louis Rigaud, he learned membrane physical chemistry and developed atomic force microscopy for the study of native membranes. As junior research director (2007−2012), he set up his lab at the Institut Curie in Paris, France. Next, he built a larger independendent laboratory at INSERM/Aix-Marseille Université (2012) in Marseille, France, where he was promoted to senior research director (2012-2016). He then moved to Weill Cornell Medicine, New York, USA (2017), where he got appointed as Professor of Physiology and Biophysics in Anesthesiology. Simon Scheuring has been awarded an INSERM Avenir

(2005), the médaille de la Ville de Paris (2007), a European Research Council (ERC) consolidator grant (2012), the grand prix Robert Debré (2013), and the NIH director's pioneer award (2019). His objective is to head a dynamic research team with members from different scientific fields ranging from biology, physics, and engineering to develop and use atomic force microscopy based technologies to provide novel insights into the processes taking place in biological membranes.