

**Characterising nanoscale heterogeneity: Controlling the transition between intermittent and non-contact regimes in tapping mode AFM**

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Nanotechnology requires the control of material properties at the molecular scale. It is a goal of imaging technologies in the field of nanoscale science to accurately and reproducibly characterise intramolecular structural heterogeneity, such as that which is particularly characteristic of complex biological polymers like proteins, glycoconjugates and nucleic acids.

Significant advances have recently been made in the elucidation of the complexities of the tip-sample interaction in one of the most commonly used Scanning Probe Microscopy (SPM) modes, tapping mode atomic force microscopy (TM-AFM) in air [1]. A major result of this work has been the prediction and demonstration of the existence of two regimes of tip-sample interaction—the one dominated by an attractive, noncontact interaction and the other by a repulsive, intermittent contact interaction. This emerging theoretical description can explain a number of hitherto puzzling effects commonly seen during TM-AFM imaging.

Here [2] we present an investigation of the criteria required for accessing the two imaging regimes, a simple method for controlling the transition between them *in situ*, and an assessment of their consequences for topographic and phase shift images of DNA and IgG antibodies. We find that the transition from repulsive to attractive regime imaging is characterised by a large increase in topographic height and concomitant decrease and sign inversion of the phase shift recorded over single molecules on mica. By varying the frequency at which the cantilever is driven, we can select which regime we wish to operate in routinely and reproducibly.

We also assess the effect of the cantilever's quality factor on accessing the two regimes in denser media or at higher scan rates using active resonance (or Q-) control [3]. Controlling the properties of the dynamic probe in this way greatly improves images of fragile nanoscale structures such as single molecules and permits us to explore the possibility of applying techniques developed in air to fluid environments.

[1] Garcia R and Perez R 2002 *Surf. Sci. Rep.* **47** 197–301

[2] Round A and Miles M 2004 *Nanotechnology* **15**, S176-S183

[3] Tamayo J, Humphris A and Miles M 2000 *Appl. Phys. Lett.* **77** 582-584