Probing the hydrophilicity of a single molecule

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Water is an essential molecule for life, while DNA is the molecule that holds the code for life. The intimate connection between water and life is related to the fact that interactions with water provide biological systems with their structure and functionality, and in particular mediate their dynamics [1-3]. Still, single biomolecular wetting is not completely understood. Here, we use insights into the mechanism of height formation in atomic force microscopy (AFM) to probe the wettability of the double-stranded (ds) DNA backbone under highly moisturised conditions. We deduce partial exposure of the hydrophobic core suggesting a possible mechanism for hydrophobic-hydrophobic interactions between hydrophobic molecules and dsDNA.

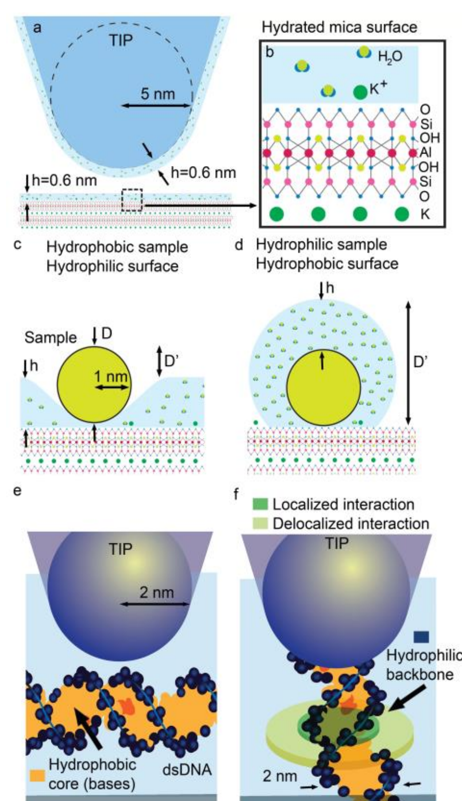

FIG. 1 Schemes of: a) the tip of an AFM in hydrated air, b) the molecular structure of a hydrated mica surface; the interaction of c) a hydrophobic sample sphere or molecule on hydrated mica surface and d) a hydrophilic sample sphere or molecule on a non-hydrated mica surface respectively and e) an AFM tip interacting with a dsDNA molecule. In e) the orange part indicates the hydrophobic (core) of the dsDNA molecule, while the dark blue regions show the location of the hydrophilic sugar-phosphate backbone. In f) the scheme exemplifies that for an ultra-sharp AFM tip, i.e. R≤ 5nm, and when the tip is above the molecule, the tip-molecule interaction is highly localised (dark green region) while the tip-surface interaction is delocalised (light green region).

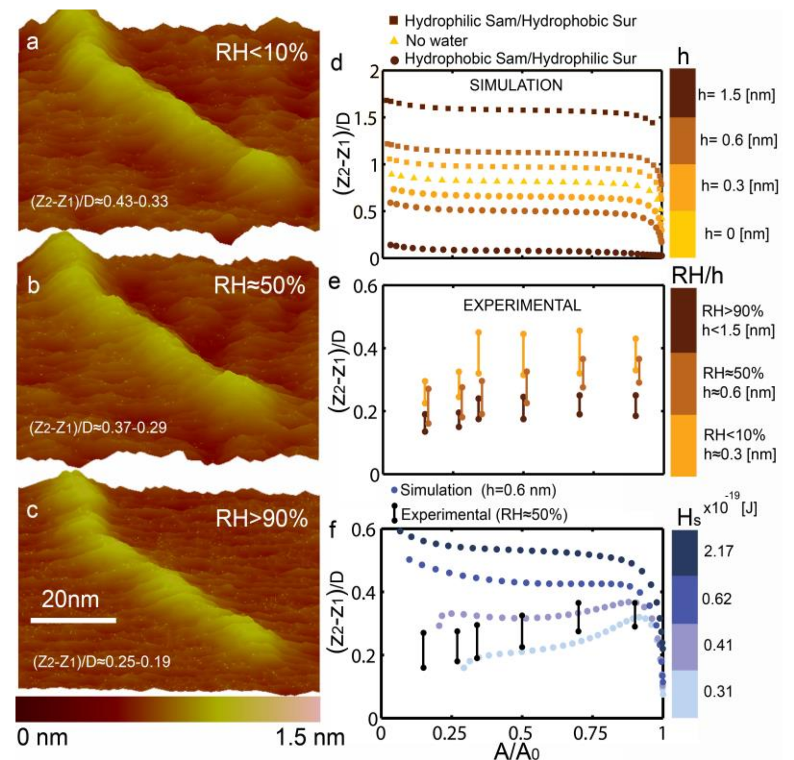

FIG. 2 a,b,c) Topography of a dsDNA molecule (800bp long) on a mica surface for a range of RH. The range of apparent heights is shown in the bottom right corner. An AFM free amplitude of A_0=2 nm and an oscillation amplitude of A≈1.8 nm has been used to obtain these images. d) Simulated apparent height $(z_2-z_1)/D$ versus oscillation amplitude A/A_0 for a range of RH and corresponding water layer thickness on mica, for a hydrophilic sample (squares) and a hydrophobic sample (circles) of true height D=2 nm. e) Experimental values of $(z_2-z_1)/D$ versus A/A_0 for a range of RH corresponding to a-c). f) Simulations (blue squares) of $(z_2-z_1)/D$ with A/A_0 for a range of H_s (Hamaker constant for the sample) versus experimental values (black circles). The fit indicates that H_s≈0.3-0.4×10-19 J.

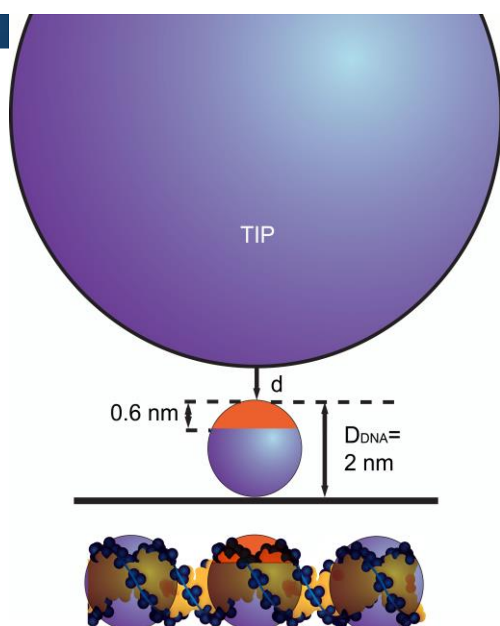

FIG. 3 Scheme of the geometry of the tip-sample interaction drawn to scale. Here the dsDNA molecule is modelled as a sequence of spheres of diameter 2 nm. The tip is positioned on top of the highest parts of one the helices, i.e. the minor groove, with a helical pitch of 2 nm. here the spheres are spaced 3.3 nm from centre to centre. This corresponds to the helical pitch of B-Form dsDNA.

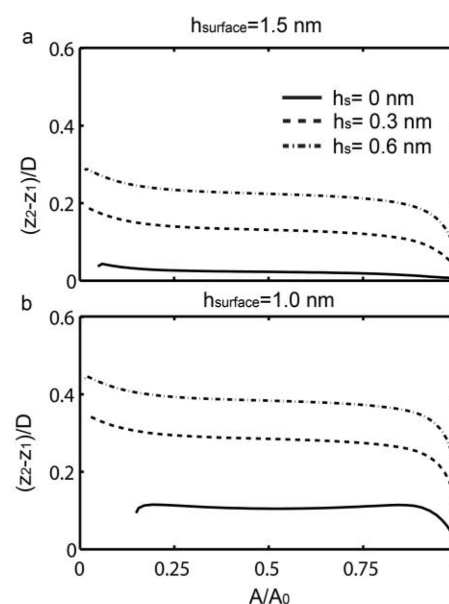

FIG. 4 Normalised apparent height $(z_2-z_1)/D$ versus oscillation amplitude A/A_0. Even for very large values of water on the surface, i.e. $h_{surface}$=1.5 nm in a), the apparent height easily reaches $(z_2-z_1)/D$~0.15-0.2 if h_{sample}=0.3 nm (i.e. one full monolayer of water covering the molecule). This corresponds to approximate 0.3-0.4 nm. For more moderate, even though still high, values as in b) where hsurface=1 nm, $(z_2-z_1)/D$~0.3 if h_{sample}=0.3 nm. This corresponds to approximately 0.6 nm.

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