LABEL-FREE DETECTION OF DNA HYBRIDIZATION BASED ON HYDRATION INDUCED TENSION IN NUCLEIC ACID FILMS

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The change in the structural and dynamic properties of water at nanoscale is crucial in a wide variety of phenomena, from the stability of a sandcastle[1] to the structure and function of nucleic acids and proteins[2]. Advances in nanotechnology, in particular those based in micro- and nanomechanical sensors, can potentially be used to analyze the role played by water molecules in macromolecular interactions[3]. Here we show that adsorption of water on a highly-packed self-assembled monolayer (SAM) of single stranded (ss) DNA has an extraordinary effect on the intermolecular interactions. We have followed the process by measuring the nano-scale bending of a silicon microcantilever, on which the ssDNA monolayer is attached, under controlled relative humidity. More importantly, the hydration-induced tension pattern undergoes dramatic changes when complementary and single mismatched DNA hybridizes with the ssDNA monolayer. To gain insight into the hydration-driven intermolecular interactions, the electrostatic contribution of the DNA backbone was studied by means of parallel experiments in which a SAM of the DNA analogue peptide nucleic acid (PNA) was used. In both cases, the features of the cantilever response to hydration and hybridization were qualitatively similar. This suggests that the tension of highly packed nucleic acid films is governed by hydration forces. Based on these new phenomena we have developed a novel nucleic acid biosensor with two key features: its optimal specificity (one mutation or single-nucleotide polymorphism, SNP) even at working temperatures much lower than the hybridization temperature of the probe-target pair, as well as its outstanding sensitivity (in the sub-picomolar range, at least ten times more sensitive than the label-dependent DNA microarrays)[4].

References:

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Figures:

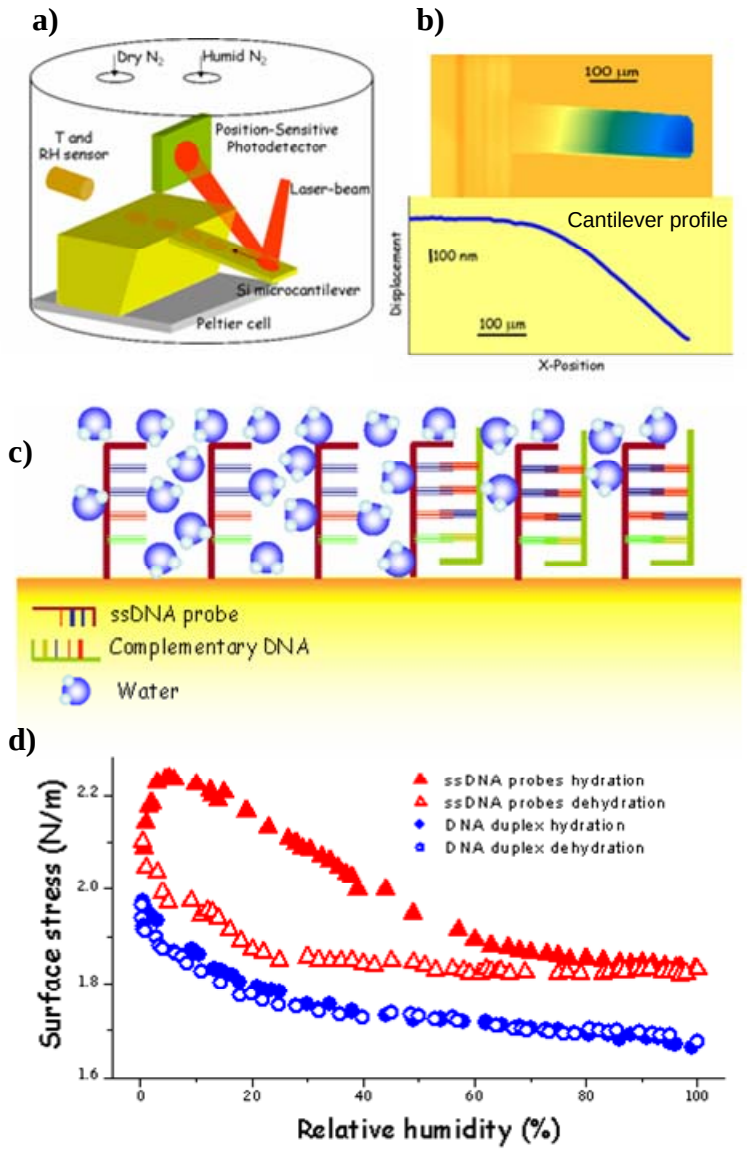

Fig. 1. a) Schematic depiction of the experimental set-up. The cantilever is placed in a humidity-controlled chamber. The relative humidity (RH) was controlled by adjusting the ratio between dry and water saturated nitrogen. **b)** The cantilever profile was obtained by scanning a laser beam over the cantilever and measuring the reflected beam deflection by a position-sensitive photodetector. A three dimensional image of the cantilever obtained by this technique is also shown. The Z dimension (deformation of the cantilever) is represented by a colour scale bar. **c)** A cartoon of the ssDNA oligonucleotides on the gold-coated side of the cantilever is shown. **d)** Surface stress measured under hydration and dehydration cycles for the cantilever sensitised with the ssDNA probes and for the same cantilever after hybridization upon exposure to a solution containing the complementary ssDNA target. We obtain a qualitatively distinct signal when hybridization occurs on the cantilever surface.