

AFM-based single molecule force spectroscopy study of nucleic acid-protein Interactions

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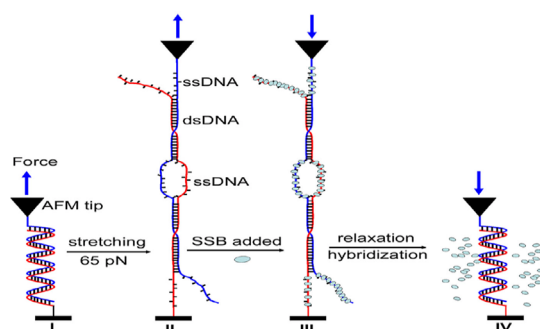
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Nucleic acid-protein interactions exist in almost every step of the central dogma. The investigation of the mechanism of such interactions at single molecule level will deepen our understanding on many important life processes such as DNA replication.

Atomic force microscopy (AFM)-based single molecule force spectroscopy (SMFS) can be used to directly detect intra- or intermolecular interactions of individual molecules as well as mechanical properties of single synthetic polymer (such as polyvinyl alcohol, polyisoprene) and biopolymers (such as titin and DNA). Such quantitative information at the single molecule level revealed the nature of some important molecular interactions. ^[1-5]

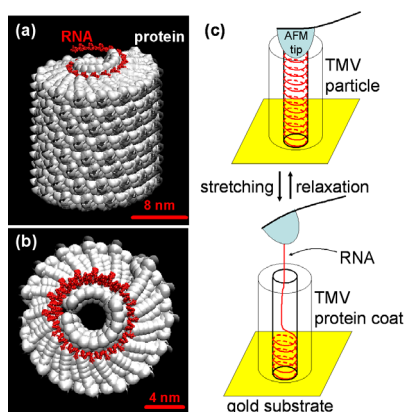
Here I will present two examples on our recent AFM study of nucleic acid-protein interactions. Namely, DNA-SSB (single stranded DNA binding protein) and RNA-TMV coat protein interactions.

As a first example, I will talk about our study on the nature of force-induced conformational transition of double stranded DNA under external force. ^[6] Our results show that during the so-called B-S transition (at about 65 pN), dsDNA is partially melted producing some ssDNA fragments, which are able to be captured by SSB proteins causing a big hysteresis between the stretching and relaxation curves. During the relaxation, the melted part of dsDNA fragments could re-hybridize resulting in the detachment of SSB proteins from them, as shown in Scheme 1.



Scheme 1. Possible model for force-induced conformation transition of a dsDNA and SSB-ssDNA interactions. ⁶

As the second example, I will present our recent study on RNA-coat protein interaction in an intact tobacco mosaic virus (TMV) by pulling the RNA genome out of its protein coat (Scheme 2).^[7]



Scheme 2. (a) Structure of TMV (~1/17 of the total length), (b) its cross section, and (c) schematic illustration of the SMFS experiment on RNA stretching.⁷

Keywords: single molecule force spectroscopy, DNA-binding protein, force fingerprint, nucleic acid-protein interaction

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