Towards a molecular dynamics description of the mechanical properties of antibodies as measured with a force microscope

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Abstract
The antibodies are key elements of the immunological system. A better understanding of their nanomechanical properties could enable to exploit all of their targeting properties. Recent developments in force microscopy such as multi-frequency atomic force microscopy (AFM) provide information about the nanomechanics of proteins [1, 2]. The AFM has several features that are attractive to the biologists. First, it is a tool with molecular resolution that enables imaging in physiologic-like environments [3] and secondly it also provides nanomechanical and chemical information at time scales relevant for bio-molecular interactions [3].

Dynamic AFM images [1] of biological molecules on ambient conditions (liquid) are controlled by nonlinear tip-sample interaction, the cantilever dynamics and the feedback control. In order to extract accurate information about topography and materials properties, these effects have to be taken into account simultaneously. So far, these experiments have been analyzed using simple models based on continuum mechanics [1]. In order to address the ultimate spatial resolution and force sensitivity of the AFM on biological molecules we model an AFM experiment on the human immunoglobulin G (IgG) by performing classical atomistic molecular dynamics simulations. The tip and the supporting substrate for the IgG adsorption are modeled as a capped carbon nanotube and as a slab of graphite, respectively. The inter- and intra-molecular forces used throughout all our simulations are the ones presented in well tested AMBER[4] (Assisted Model Building with Energy Refinement) force field suite. The tip and substrate force-fields are built using the antechamber tool (present in AMBER) and then these parameters are fine tuned to reproduce the correct[5] crystallographic and mechanical properties of the tip and the substrate.

These simulations provide an insight into the atomistic mechanisms controlling the local deformation (induced by an AFM tip) of the protein and also allow us to map the mechanical response of a protein on to its structure (amino-acid sequence).

References
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Figures:

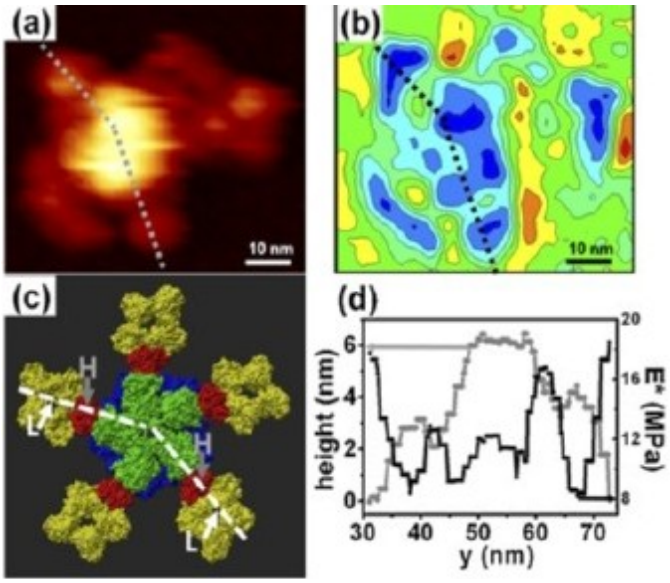

Figure 1. Figure from Ref.[1]. Topography and flexibility map of a single IgM antibody. (a) Bimodal FM AFM image . (b) Flexibility map obtained simultaneously with the topography image. (c) Pentamer structure of the IgM antibody. The locations of the lowest (L) and highest elastic moduli (H) are marked. (d) Topography (grey) and flexibility (black) profiles along the lines marked, respectively, in (a) and (b).

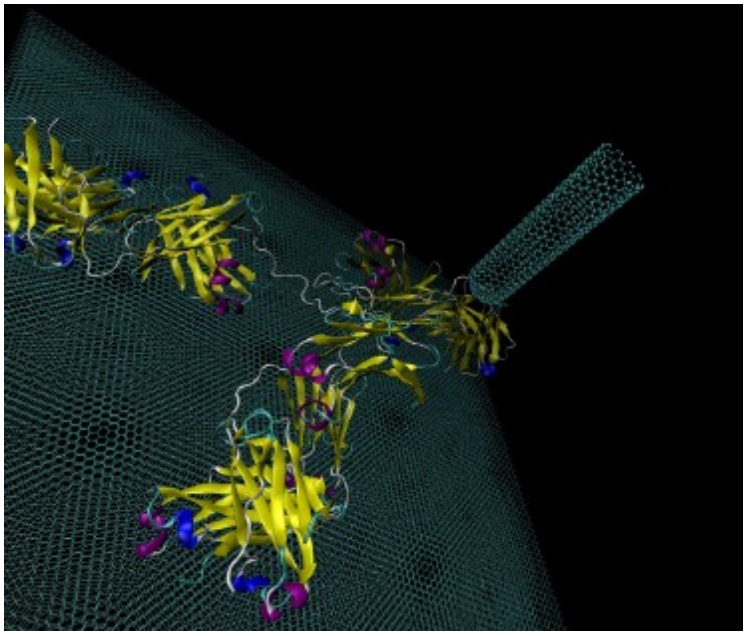

Figure 2. Schematic representation of Human immunoglobulin G over a graphite slab. It is also represented the capped carbon nanotube that will serve as our AFM tip.