Templated virus deposition: from molecular-scale force measurements to kinetic Monte Carlo simulations

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ABSTRACT

The use of macromolecular scaffolds for hierarchical organization of molecules and materials is a common strategy in living systems that leads to emergent behavior. Here we describe an effort to relate interaction force measurements between viruses and modified substrates to the energy landscape during virus assembly on surfaces. Potentials and binding energies are then used in kinetic Monte Carlo simulations to predict assembly morphology under controlled conditions replicated experimentally. We use atomic force microscope (AFM) tips functionalized with specific chemical species to measure interactions in the assembly system, which includes Cow Pea Mosaic Virus (CPMV). CPMV virus particles were engineered to express specific functional groups to modulate the strength and kinetics of interactions and assembly morphology. We show that the CPMV morphological evolution predicted by the simulations correlates with AFM observations.

Keywords: virus, force, monte carlo, energy, assembly

1 RESULTS AND DISCUSSION

One advantage of using macromolecular scaffolds for hierarchical organization is that it generates micron-scale structures from nm-scale building blocks possessing high-density functionality defined at Å-scales by active sites, typically on proteins complexes such as viral capsids. Figure 1a shows a model representation of CPMV self assembled virus on SAM modified gold substrate (Figure 1b).

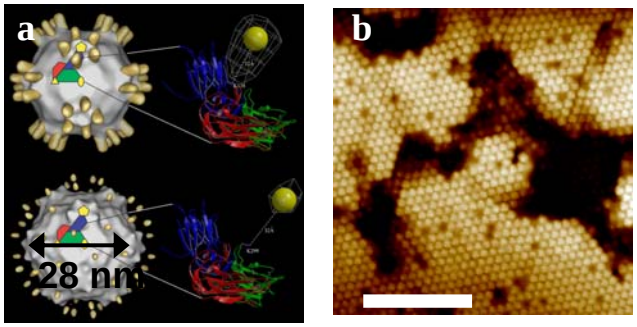

Figure 1: Model of CPMV virus (http://johnsonlab.scripps.edu/research/images/) and AFM image of self assembled CPMV virus on a gold substrate (scale bar = 500 nm).

Using interaction force measurements between viruses and modified substrates to derive the energy landscape during virus assembly provides a means to explore the nature of the governing interactions and to investigate the role of solvent interactions on inter-viral potentials. The virus are specifically engineered to express various functional groups on its surface that can be used for attachment and/or patterning on templated substrates to guide the virus assembly (Figure 2).

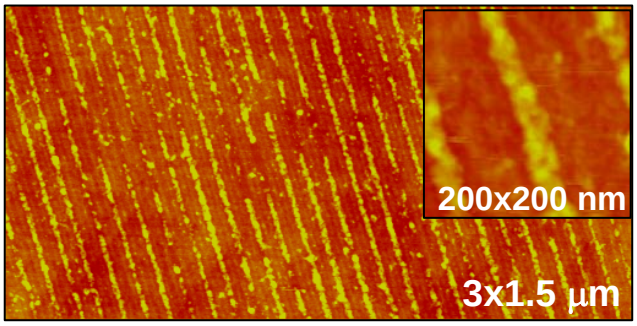

Figure 2: AFM image of a chemically modified trenches on a SAM background to form an array of line template for bonding to CPMV cys modified virus.

The experimental configuration to measure force curves and image surfaces is schematically shown in Figure 3, along with a typical force curve derived between –SH modified and AFM tips and cys-modified-CPMV attached to the surface.

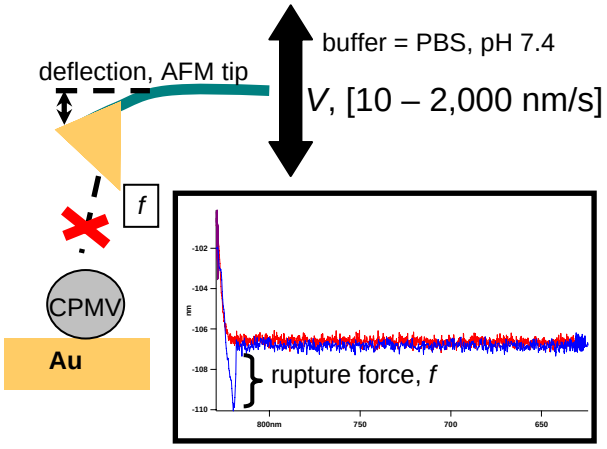

Figure 3: Schematic of force measurement setup indicating AFM tip pull off rates and bond breaking for a given rupture force.

The results of repeated force measurements describe a stochastic process [1] that depends on the pull-off rates of the tip (rate = $k_s \times v$ N/s), which, in turn, depends on the spring constant of the cantilever/tip, k_s, and the linear velocity of the tip, v, as it approaches and retracts from the CPMV virus attached to the surface. Preliminary measurements made between dithiolbezene (DTB) modified surfaces on gold covered tips and surfaces are shown in Figure 4.

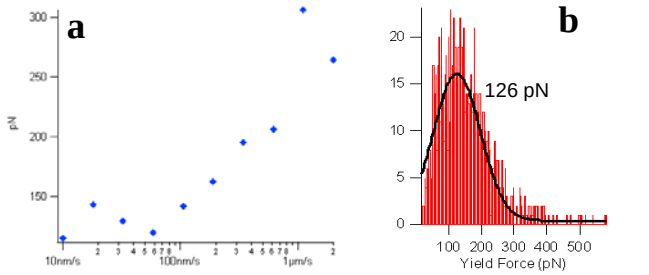

Figure 4: Force spectrum (a) and distribution (b) measurements for DTB modified surfaces.

Analysis of the force spectrum in Figure 4 indicates a distance to the transition state along the reaction coordinate of 0.12 nm during bond breaking and a binding energy on the order of $\Delta G=6k_BT$.

Monte Carlo simulations of the binding of viruses to modified surfaces are shown in Figure 5, along with the AFM images of viruses deposited on templated substrates (Figure 2). These simulations relate binding strength (Figure 4) to specific patterning features which correlate with observed CPMV virus assembly patterns. This model description provides thus a means to tune the assembly of CPMV virus by modifying attachment parameters through chemical and biochemical modification and achieve arbitrary patterns on the nanoscale.

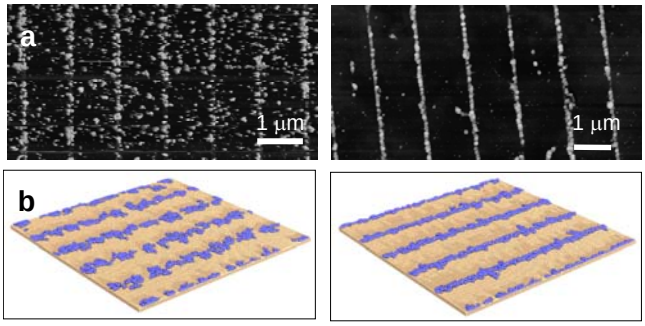

Figure 5: (a) AFM images of patterned CPMV virus and (b) corresponding Monte Carlo simulation of the virus assembly on templated surfaces.

2 TEXT FORMAT

The title should be in boldface letters centered across the top of the first page using 14-point type. First letter capitals only for the title. Insert a blank line after the title, followed by Author Name(s) and Affiliation(s), centered and in 12 point non-bold type. The paper begins with the abstract and keywords followed by the main text. It ends with a list of references.

REFERENCES

[1] Evans E and Ritchie K 1997 *Biophys J* **72** 1541-55