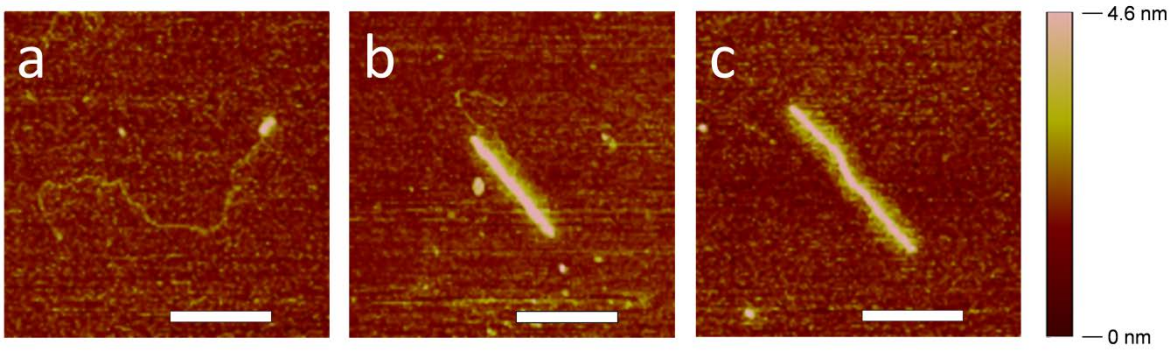
Supramolecular Design of a Minimal Coat-Protein for an Artificial Virus

Virus particles are highly effective vehicles to deliver genetic material into susceptible host cells. A necessary condition highlighted by theoretical models for the successful formation of infective virus particles is precisely tuned co-operativity of the self-assembly process. There have been many attempts to construct self-assembling virus-like particles but to date the key property of cooperativity has not been explicitly incorporated in any design of artificial viruses. Here we show the rational design of a minimal viral coat protein based on three simple polypeptide domains which do feature precise control over the co-operativity of its co-assembly with single DNA molecules into rod-shaped virus-like-particles (VLPs). We use polypeptide domains that previously we have used for a range of hydrogel-forming polypeptides, and which are inspired by natural structural proteins such as silks and collagens. The triblock polypeptides are produced by secreted expression in the yeast *Pichia Pastoris*. We confirm the validity of our design principles by showing that the kinetics of self-assembly of our VLPs follows our previous model for Tobacco Mosaic Virus (TMV) assembly. Mature VLPs protect DNA against enzymatic degradation and transfect cells with considerable efficiency, making them promising scaffolds for delivery vehicles. Being biosynthetic and protein-based, our design also paves the way for developing viruses that are completely artificial and yet can replicate in a cellular host.



Nucleated growth of VLPs formed by artificial capsid proteins, templated by 2500 basepair linear double stranded DNA. Representative AFM images (in air) of VLPs adsorbed on silicon. DNA concentration 10μg/ml, protein concentration 300μg/ml. Bar = 200nm. Incubation times: a) 10 min b) 5h 50min c) 24h.