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A MINIMAL ARTIFICIAL VIRAL COAT PROTEIN

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Viruses are among the simplest biological systems and may therefore present a possible stepping stone towards artificial life. In order to understand the fundamentals of viral coat assembly, and in order to eventually create efficient man-made delivery vehicles, we have attempted to design an artificial viral coat protein with minimal sequence complexity. At the very least, the protein should reproduce the cooperative encapsulation of single nucleic acids that is so typical for viral capsid proteins. From a functional point of view, parts of viral capsid proteins are involved in nucleic acid-binding, parts in protein-protein interactions that give rise to cooperativity, and parts in regulating interactions with the outside world. We have encoded these functionalities in three polypeptide blocks, each having minimal sequence complexity: the binding domain is an oligolysine, protein-protein interactions are encoded by repeats of silk-like octapeptides. As for regulating interactions with the outside world, we use a long hydrophilic polypeptide block for simple shielding. The triblock polypeptides are produced via recombinant DNA technology and expressed at a large scale in yeast. When complexed with DNA, the triblock polypeptides produce remarkably regular single nucleic-acid, rod-like complexes via a cooperative assembly kinetics that is completely analogous to that of TMV virus particles, as we show using a theoretical analysis. Inside the artificial virus particles, DNA is protected from enzymatic degradation. Toxicity of the artifical virus particles was found to be very low, while at the same time, their transfection effeciency for HeLa cells is already equal to the commercial standard Lipofectamin. We conclude that these minimal viral coat proteins are both interesting as a model system for fundamental studies of viral assembly and as a scaffold for future biosynthetic delivery vehicles.

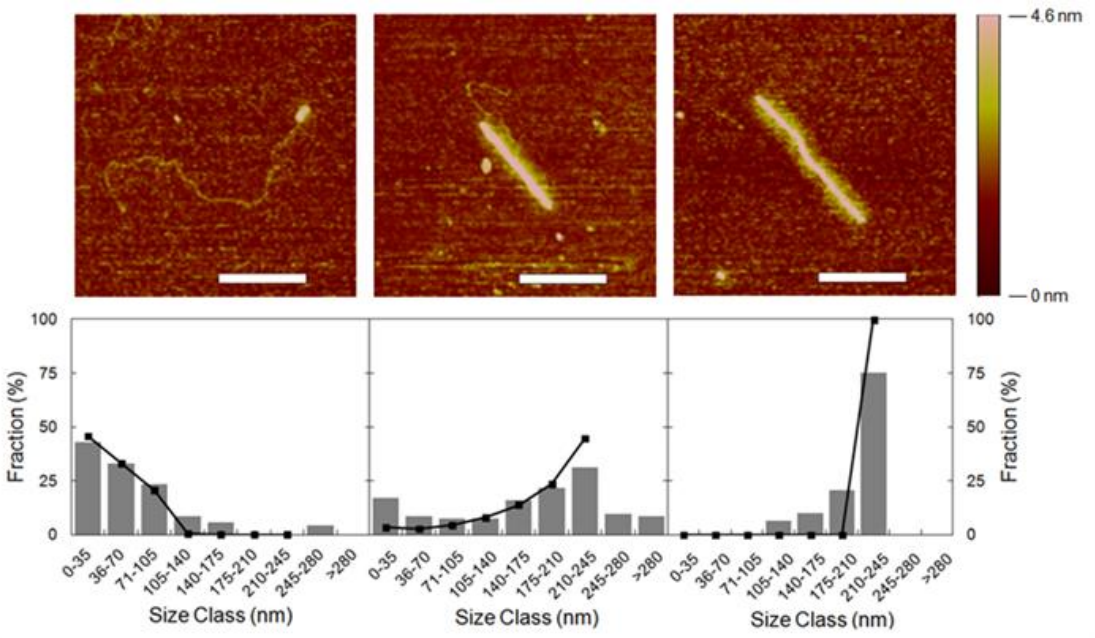

Figure:kinetics of assembly of artificial viral coat protein with 3kb linear DNA. Top row: representative AFM images of dried complexes after 10min, 5h50min and 24h of incubation, ratio of negative DNA phosphate charges (P) to positive charges on the nitrogens of polylysine binding domain (N): N/P=3. Bottom row. corresponding distribution of encapsulated length. Bars: from AFM images, black line: fitted with kinetic theory that was previously used to analyze TMV particle growth.