Growth Dynamics of a Self-Replicator Characterised by High Speed-AFM

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Self-replication is widely accepted to be an essential process in (the early stages of) life. We recently discovered a new mechanism of self-replication, driven by self-assembly, where replicators grow out of a complex mixture of interconverting molecules. Specifically, small synthetic peptide-based building blocks have been developed which react to give a mixture of different macrocycles of which one particular ring size self-replicates, driven by its assembly into fibres. Still it remains poorly understood how these replicators, from monomeric far-from-equilibrium states, form close to thermodynamically equilibrium supramolecular structures. Here we were able to visualize self-replication for the first time, using real-time High Speed-Atomic Force Microscope (HS-AFM, fig. 1) in combination with molecular dynamics (MD) simulations. These studies revealed several unexpected events which seem to control the replication process. While a seed (a preassembled short fibre of replicating hexameric macrocycles) in a controlled environment can initiate a rapid growth of the replicator fibre, there are several additional factors essential to the replication process. Firstly, a molecular complex composed of "food" (a mixture of monomer and small non-replicating macrocycles) needs to be attached to the side of the fibre. Secondly, for a successful rapid growth, the food should either attach to the extremity or have sufficient mobility to undergo 1D directed diffusion towards the end of the fibre. Interestingly, the probability for the food to attach to the extremities is much higher than to attach in the middle, indicating a more favourable interaction energy at the fibre end. Once a successful food to fibre arrangement is established, the fibre will show rapid growth (i.e. replication) at an average rate of ~4 nm/s, consuming the attached food. In conclusion, real-time observation of the process of self-replication has yielded unexpected insights into the process of self-replication, also revealing a new mechanism of self-assembly.

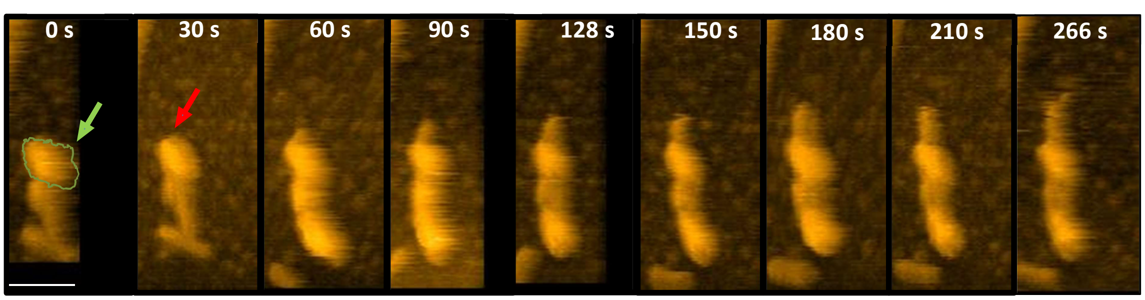

Figure 1. *Real time growth of a peptide functionalized macrocyclic self-replicator observed under HS-AFM. Green arrow showing the attached food, and the red arrow indicating the fibre growth. Scale bar 20 nm.*