Force exertion by light-fueled self-assembly

Cissé, Nicolas

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university of groningen

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Synthetic polymer motors

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by

Nicolas Cisse

born on 3 November 1992
in Rennes, France

Supervisors

Prof. T. Kudernác
Prof. W.R. Browne

Assessment Committee

Prof. S. Otto
Prof. A.J. Minnaard
Prof. J. Montenegro

Aim and outline

Vital cellular functions rely on dynamic soft materials known as microtubules and actin filaments. The role of these polymerization motors consists in converting the free energy of supramolecular polymerization into mechanical forces, through which purposeful motion can be generated, for example chromosomes separation or cell movement.
The goal of this PhD project is to create fully artificial and waste-free polymerization motors capable of converting light into mechanical forces at the nanoscale and beyond. The first challenge is to control the aqueous supramolecular polymerization of dynamic tubular self-assemblies (artificial microtubules) and dynamic networks of helical supramolecular polymers (artificial actin networks) by light. The second challenge is to demonstrate the exertion of mechanical forces exerted by their light-fueled self-assembly.

Chapter 1 reviews the use of molecular self-assembly processes for the exertion of mechanical forces and work. First, the basic mechanistic principles of how the mechanical force can be exerted by supramolecular polymerization and depolymerization are discussed. This is followed by the description of the biological polymerization motors and how these machineries were reconstituted in the artificial context. Finally, we discuss fully synthetic self-assembling systems that in part address challenges on the way towards artificial polymerization machines including a perspective on where this research should go.

In **Chapter 2** we demonstrate cyclic peptide nanotubes with non-equilibrium steady states that are fuelled by light via the photoacid-mediated protonation of carboxylic acid residues. Light intensity is used to control the speed of the assembly processes. This supramolecular system operates continuously and repeatedly, without any waste, and demonstrates a dynamic behaviour that is key to the operation of artificial polymerization machines. We take onto the challenge of harnessing the self-assembly of cyclic peptides to exert pushing forces. We demonstrate that the movement of microbead cargo, confined in water-in-oil droplets, can be controlled by the pH-responsive self-assembly of cyclic peptide nanotubes. We discuss the limits of this approach, and we conclude that the synthesis and characterization of new molecular building blocks, intrinsically photo-responsive, is required to demonstrate the biomimetic mechanism of force generation e.g., Brownian ratcheting.

In **Chapter 3** we demonstrate giant nano-ribbons and tubules with non-equilibrium steady states that are fuelled by light. We present the design, synthesis, and characterization of linear peptide building blocks that are decorated with photo-responsive moieties. We investigate the most important thermodynamic and kinetic aspects of their (de)polymerization through various spectroscopic, microscopic, and rheological techniques. In particular, we demonstrate a light-fueled depolymerization mechanism that is key to the operation of artificial actin filaments.

In **Chapter 4** we harness the pulling forces exerted by the light-fueled disassembly of peptide based supramolecular ribbon networks. The pulling forces drive the clustering of microbeads that are multivalently bound to the disassembling ribbons. The re-assembly of the ribbon networks does not push the beads apart, so that the light-fueled disassembly cycles can drive the process of microbeads clustering forward i.e. processively. We demonstrate pulling forces operating at length-scales that can be modulated by molecular design of the building blocks.

In **Chapter 5** Beyond light-fueled hydrogelation, we demonstrate the first light-fueled hydrogelator that also acts as an effective photoacid at the supramolecular level, i.e. supramolecular photoacid. The proton-catching reaction is the supramolecular polymerization of the azobenzene-peptide into β-sheets (ribbons) under visible light irradiation, and the proton-releasing reaction is the UV light-fueled depolymerization of the ribbons. The β-sheets within the hydrogel consist in a reservoir of protons which are released/caught on demand by light-fueled disassembly of the ribbon network. Therefore, gel-sol transitions are associated with tunable and reversible pH changes. pH and stiffness are modulated in synergy with spatio-temporal control in a non-contact and waste-free manner. This concept may find applications in biotechnology, for example the pH change could be harnessed to locally activate a pH-responsive drug during its release from the gel. Here as a proof of principle, we trigger the color change of the pH-indicator Bromothymol blue, allowing to visualize the pH profile of the system during the light-fueled disassembly of the transparent hydrogel.

Chapter 6 describes the discovery of biased macroscopic motion emerging from the shear anisotropy of peptide ribbons hydrogels. We explore the asymmetric mechaniscs of twisted versus helical ribbon networks through shear rheology. We investigate and hypothesize on

the mechanism of this unpresented transfer of asymmetry from the nano up to the macro scale.

In **Chapter 7** we demonstrate giant nano-sheets emerging from the hierarchical co-assembly of cyclic peptides. Due to their high versatility, D-,L-α cyclic peptides are promising building blocks for the fabrication of various bottom-up nano/micro-objects and supramolecular machines.

In **Chapter 8** we demonstrate the light-fueled 1D to 2D supramolecular polymerization of cyclic peptides nanotubes. We present the design, synthesis, and characterization of cyclic peptide building blocks that are decorated with photo-responsive moieties. We investigate the most important thermodynamic and kinetic aspects of their (de)polymerization through various spectroscopic and microscopic techniques.

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