Supramolecular Assembly by Computational Microscopy and Spectroscopy

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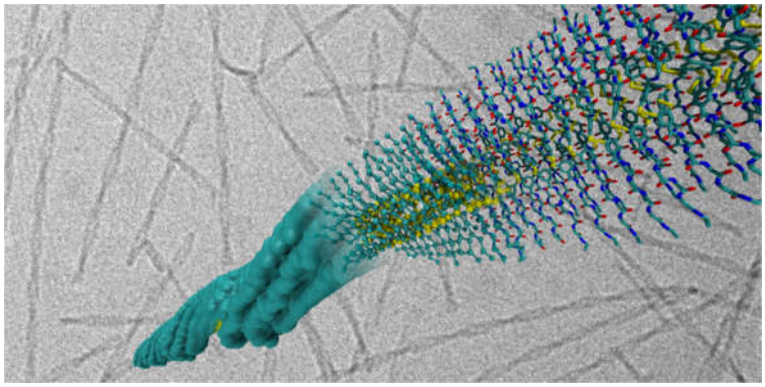
The importance of supramolecular polymerization and self-assembly in both Nature and material science has nowadays been fully recognized. The pathway toward complete control over non-covalent synthesis of nanostructures and molecular machines can be found through the exact understanding of atomic-resolution interactions between individual building blocks. Traditionally, such details are only available through molecular simulations ("computational microscopy"), which are now able to deal with millions of atoms and timescales up to microseconds.[1] On the other side, single molecule techniques, spectroscopy and advanced microscopy (electron and atomic force) are evolving toward better and better spatial and time resolution from the top down.

In this work, we will demonstrate how the two approaches can meet in determining the dynamic growth of a self-replicating peptide macrocycle fiber. The static structure of the fibers was demonstrated using Molecular Dynamics, quantum chemical, TEM, (2D)IR, and CD techniques.[2] Subsequently, we have probed the growth of the self-assembled fibers using a dynamic MD "docking" approach and high-speed AFM experiments on a membrane in aqueous solution. An unexpected variant of the 'dock-lock' mechanism was discovered to be responsible for the growth of the supramolecular polymer.



The self-assembly of bio-inspired supramolecular polymers can be unraveled using molecular dynamics simulations combined with experiments.[1]

1. Frederix, P. W. J. M., Patmanidis, I. & Marrink, S. J. Molecular simulations of self-assembling bio-inspired supramolecular systems and their connection to experiments. *Chem. Soc. Rev.* **47,** 3470–3489 (2018).

2. Frederix, P. W. J. M., Idé, J., Altay, Y., Schaeffer, G., Surin, M., Beljonne, D., Bondarenko, A. S., Jansen, T. L. C., Otto, S. & Marrink, S. J. Structural and Spectroscopic Properties of Assemblies of Self-Replicating Peptide Macrocycles. *ACS Nano* **11,** 7858–7868 (2017).