Designer DNA nanoparticles for spatially-oriented macromolecular assemblies

Dr. **Rémi VENEZIANO**, post-doc associate

Biological Engineering Department, Laboratory for computational Biology and Biophysics,
MIT Massachusetts Institute of Technology, Cambridge MA, USA

Organizing macromolecules at the nanometer scale to mimic specific cellular assemblies will enable a better understanding of natural molecular mechanisms and potentially allow the synthesis of new biomimetic systems. In the last several years this formidable challenge has been partially addressed with the emergence of DNA as a promising material that can be specifically programmed at the nanometer scale to scaffold nanoarchitecture assemblies. More recently DNA origami nanostructures have demonstrated major potential to serve as a versatile medium to program and organize complex molecular architectures at the nanoscale. These spatially addressable DNA nanostructures with finite size have been used in various applications such as enzyme cascade reconstitution, membrane nanopore formation, delivery vehicles, and excitonic devices, among others. While potential applications of these objects have grown significantly during the last couple of years, their manual design and their increasing complexity have limited this technology to experts in the field. To respond to this, we have developed a fully automated top-down approach to easily design and directly synthesize arbitrary programmable 3D DNA nanoparticles that can be used by non-experts, needing only a user-defined geometry as input. The characterization methods used, including cryo-electron microscopy and atomic force microscopy, show robust and monodisperse nanoparticles with well-defined 3D structures. These particles are stable in a variety of physiological buffers and are easy to modify, offering a real alternative to reconstruct complex macromolecular assemblies to enable diverse biological applications such as targeted drug delivery or excitonic circuits.