Structure determination of an artificial virus made of self-assembling cyclodextrin and dsDNA by cryo-EM (Cyclo-Cryo)

Stage Master M2

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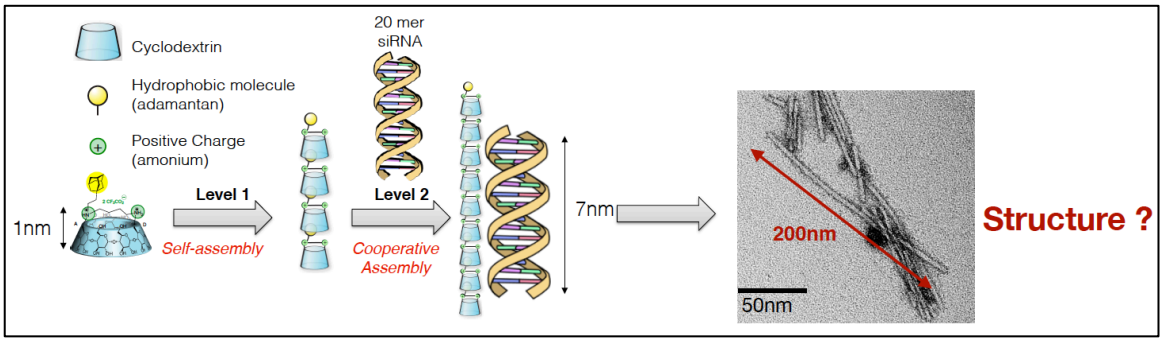
Nature makes beautiful architectures such as microtubules, fibrils, helical or icosahedral viruses… These homogeneous assemblies could never be reproduced artificially, until we recently observed one by mixing modified cyclodextrins and DNA. (see figure)
In a preliminary work, we have characterized, using biophysical experiments and visualized, using electron microscopy, the DNA/Cyclodextrin complex. Long and rigid fibers were observed with a constant diameter ca. 6 nm and lengths of hundreds of nanometers, which is much bigger than the individual bricks of this assembly (20mer DNA=7nm, Cyclodextrin D=1nm).



The first objective of this master project is to calculate the 3D structure of the 1st co-assembly CD+20mer DNA at the highest possible resolution of the 1st co-assembly from the images already available taken from the Krios Titan 300kV.
The second objective is to fit the atomic structures into the Cryo-EM 3D map. In this task, in silico simulation methods will be applied to refine the structure of the assembly so that it closely fits in the electron density map obtained by cryo-microscopy analysis. This will help us to describe in great details the architecture of the assemblies and the precise interactions between the various molecules inside the assemblies. The fitting refinement to the electron microscopy map is a crucial step that usually requires the introduction of structural flexibility to obtain a reliable solution. We will use our new tool called MDeNM-EMfit which combines MD simulations and the excitation of intrinsic motions given by Normal Mode Analysis.
This master 2 study is perfectly integrated in the ultimate goal of our project, which is to predict a shape of a hierarchical homogeneous self-assembly in solution, which is currently totally out of reach. We will then use this knowledge for further developments in gene therapy.

References

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