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Multi-scale mass analysis for the characterization of engineered DNA assemblies

Nucleic acids (DNA, RNA, artificial analogues such as TNA) can form remarkable three-dimensional structures, which play key roles in biology and nanobiotechnology. In the field of DNA nanotechnology, static or dynamic nucleic acid assemblies have applications in biotechnology, nanomedicine, nanophotonics and nanoelectronics. Determining the size, shape and assembly route of oligomeric nucleic acids (like cages, Legos or DNA origami) is essential to understand their structure and to improve their rational design. Current techniques, notably gel electrophoresis, chromatography and dynamic light scattering, determine the average size of nanostructures, while atomic force microscopy and electron microscopy can assess individual particle morphology with nanometre resolution. However, these methods do not provide accurate details on the stoichiometry of folding products, intermediates in assembly pathways, nor homogeneity and stability of biomolecular assemblies in different buffers.

To fill this gap, we aim to develop a multi-scale analytical approach for characterising DNA assemblies using mass spectrometry (MS) in native mode. In particular, we propose to utilise different modalities of MS: native nano-ESI-MS, Suspended NanoResonator (SNR) and NanoElectroMechanical Sensor (NEMS). These approaches allow the investigation of a wide mass range from a few hundred Dalton to hundreds of MegaDalton. Indeed, we intend to determine masses of a variety of DNA assemblies and hybrid architectures (DNA-organic molecules, DNA-particles, DNA-proteins, etc.). In addition, we aim to synthesize functionalized architectures that can be used as standards to improve the accuracy of mass measurement in the multi-megadalton mass range. Overall, our multi-scale analytical approach will enable us to elucidate the structural composition of diverse DNA architectures, their oligomeric state, size and morphology.

User consent

yes

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