Insights into the 3D structures of sequence-defined macromolecules and DNA-templated supramolecules

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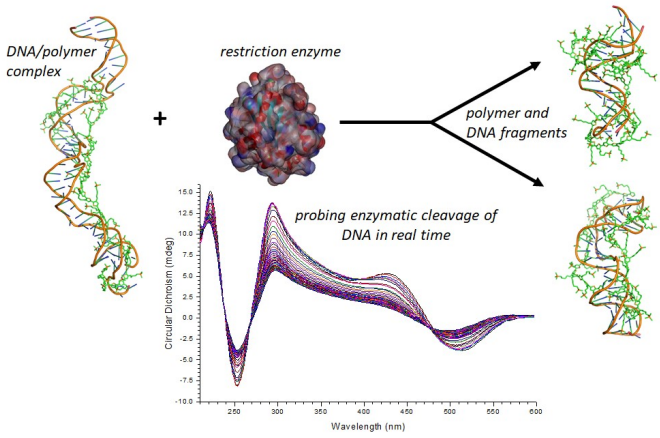
The perfect sequence- and stereo-control in biological macromolecules such as DNA and proteins imparts remarkable functions such as information storage, recognition, and catalysis. Inspired by these exquisite information-rich structures, our group aims at designing precision macromolecular and supramolecular assemblies with tailored properties for applications in health and materials sciences.[1-4] We particularly focus on the understanding of sequence-structure-properties relationships, towards a rational design of organized assemblies for specific functions. The 3D structure and (supra)molecular organization are studied through a combination of chiroptical spectroscopy, microscopy, and molecular modeling simulations, giving insights into the effects of monomers sequence, chirality, and cooperativity. In this talk, we will make a journey into our recent works on two types of bioinspired systems:

1) ***Sequence-defined macromolecules***: inspired by enzymes, for which on the precise 3D positioning of catalytic groups in the protein structure is key for the activity, discrete sequence-defined and stereo-controlled oligomers have been designed based on a poly(triazole-urethane) backbone.[4] These sequence-defined oligomers were exploited to precisely position 3 catalytic units along the chain, in view of constructing a catalytic system for the selective aerobic oxidation from alcohols to aldehydes. Remarkably, we observed that the catalytic activity varies when changing the position/order of the catalytic units in the oligomer sequence. We rationalized these results by combining molecular modeling simulations and network analysis, displaying the effect of sequence order on the 3D structures and functional connections between catalytic groups,[5] as observed for other multifunctional catalytic molecules.[6]

2) *DNA-templated supramolecules*: a way to organize (macro)molecules in space is to exploit DNA as a molecular template, as explored by us and others to construct for example, helical stacks of chromophores, photonic wires, and delivery systems.[1,2] We utilized DNA templates to guide the self-assembly of several types of π-conjugated molecules through H-bonding and/or electrostatic interactions, and we revealed their 3D structure, template effect, and cooperativity.[7,8]

Here, we discuss the example of a templated supramolecular assembly of DNA and π-conjugated polymer, a cationic polythiophene. Their complexation in solution and the effects of DNA length and sequence were explored.



Remarkably, we observed important effects of DNA sequence on the chiral induction to the polymer backbone.[9,10] We demonstrate that this can be harnessed to monitor the enzymatic activity of an endonuclease in a label-free, real-time fashion (see figure on the right).

References

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