Liquid Crystal ordering of single and oligo nucleotides: from supramolecular assembly to polymeric nucleic acids

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Abstract

One of the most crucial steps for the origin of lifeis the emergence of the first information carrying biopolymers from their monomeric constituents, conceivably available in the prebiotic era. Based on a broad experimental exploration of the collective behavior of DNA and RNA nucleotides and oligomers (oligoNA) [Nakata 2007, Zanchetta 2008, Bellini 2012, Fraccia 2016], we report recent progresses in the investigation of a pathway by which linear self-assembly and spontaneous Liquid Crystal (LC) ordering might have enhanced the prebiotic emergence of long and potentially active RNA polymers. The key features of this self-sustaining pathway are a hierarchy of base pairing and stacking, linear aggregation, phase separation of sequences and structures, driven by the LC ordering, which can select nucleic acids fragments, and template their polymerization inside compact, ordered but fluid micro-domains.

LC Self-Assembly of single and oligo nucleotides

We observed LC ordering of mononucleotide triphosphates, dNTPs and rNTPs, in aqueous solutions, resulting from selective (AT and GC) pairing and aromatic stacking of nucleobases [Smith 2018]. Within LC nucleotide pairs are kept in linear backbone-free aggregates exhibiting the key structural elements of biological nucleic acids. This behavior has been recently extended to other nucleotides species, such as RNA 5',3'-cyclic monophosphate and DNA 5'-phospho-2-methylimidazolide, whose enhanced reactivity has shown to be potentially relevant for abiotic polymerization.

LC templated non-enzymatic ligation

Inside the LC matrix, oligoNA are held in end-to-end contact to form chemically discontinuous but physically continuous double strands. When phosphate activating molecules are added (as the water soluble carbodiimide EDC), the LC templating environment strongly

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promotes the non-enzymatic chemical ligation of oligomeric DNA [Fraccia 2015] and RNA [Todisco 2018], into more than 100 base long strands and favoring the formation of linear products towards the circular ones.

Our current investigation is aimed in testing concentration and temperature cycles as promoters of the evolution of a starting random oligoNA-monomer distribution, wherein folding and potentially active sequences would be selected from the LC phase.

According to this scenario, during drying-wetting cycles LCs continuously form and melt, depending on temperature, concentration and length of the constituent molecules. Herein the supramolecular assembly guides intermolecular ligation toward the formation of long linear chains which in turn stabilize the whole self-assembly, establishing a self-sustained positive feedback loop, capable of producing potentially active RNA strands.

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