

A-type helicity controls efficient nonenzymatic template copying of nucleic acids

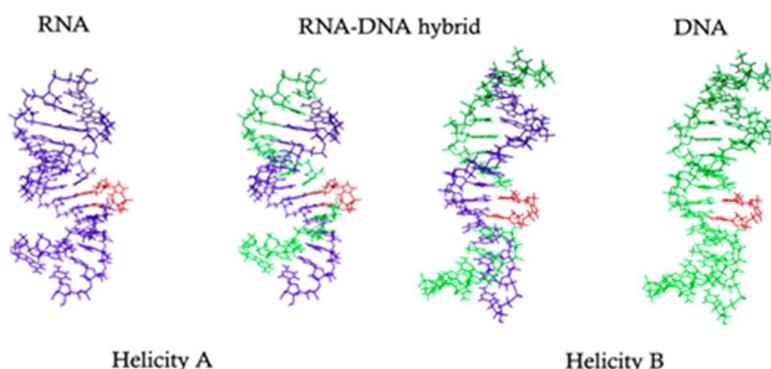
Barbara K. Lech^a, Petr Jurecka^b, Marie Zgarbova^b and Rafał Szabla^a

a) *Institute of Advanced Materials, Faculty of Chemistry, Wrocław University of Science and Technology, Wybrzeże Stanisława Wyspiańskiego 27, 50-370 Wrocław*

b) *Department of Physics, Faculty of Science, University of Ostrava, 30. dubna 22, 701 03 Ostrava*

For nearly half a century, nonenzymatic RNA primer extension has been extensively studied, revealing that imidazolium-bridged dinucleotides likely play a crucial role in this process. These findings support the hypothesis that RNA was a key molecule in the origin of life [1–3]. In contrast, DNA self-replication proceeds at a much slower rate, making it largely irrelevant for prebiotic chemistry, although it remains an interesting alternative pathway for DNA synthesis. While common techniques such as solid-phase synthesis and PCR are widely used to produce DNA, they suffer from several drawbacks, including procedural complexity, high enzyme costs, and extensive solvent consumption. Notably, recent studies have demonstrated that DNA synthesis on an RNA template is significantly faster than on a purely DNA template, possibly due to the A-helical structure of RNA [5].

In this work, we performed classical molecular dynamics simulations of DNA self-replication on an RNA template with phosphoroimidazole activation. We show that the RNA template enforces A-type helicity in the hybrid DNA/RNA duplex, in contrast to the B-type helix characteristic of purely DNA-based systems. Based on detailed structural analyses, we conclude that helix type is the primary factor governing the feasibility of nonenzymatic primer extension.



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