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Viscosity-mediated replication of an RNA duplex containing a ribozyme motif

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An important goal in origins of life research is the demonstration of an RNA system that can undergo sustained cycles of replication without the aid of protein enzymes. However, despite decades of research on prebiotic nucleic acid origins and information transfer, the community has yet to accomplish this goal. Previous studies on template-directed RNA synthesis have focused mainly on single-stranded templates and rarely consider the additional challenges associated with multiple rounds of information transfer, such as strand inhibition [1,2]. We will discuss a replication system for gene-length RNA duplexes that is enabled by a viscous solvent (Figure 1). This solvent provides a diffusion-limited environment, which promotes the formation of intramolecular nucleic acid structures, which circumvents the strand inhibition problem [3]. These kinetically trapped single-stranded structures allow the assembly of oligonucleotide substrates on both of the template strands, which can be subsequently ligated. Additionally, we demonstrate that viscous solvents can promote the replication of an RNA duplex containing a hammerhead ribozyme sequence, which is catalytically active in hydrated eutectic solvent conditions. These findings suggest that viscous solvents generated by water evaporation in day/night or seasonal cycles on the prebiotic Earth, could have provided a viable environment for replication of nucleic acid structures with complex intramolecular structures, such as ribozymes.

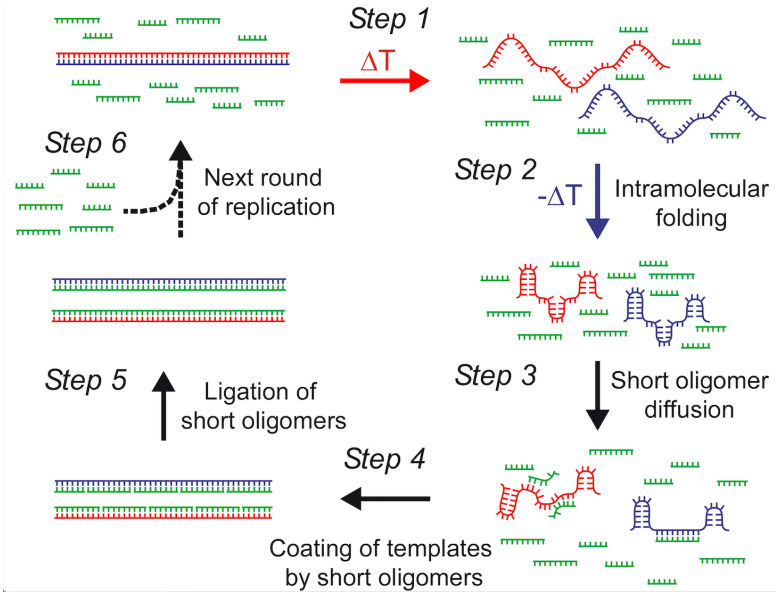

Figure 1 A model process for the prebiotic replication of nucleic acids that circumvents the strand inhibition problem. Adapted from He *et al.*, 2017 [3].

References:

[1] Joyce, G.F. & Orgel, L.E. (1986) *Journal of Molecular Biology* 188: 433-441.
[2] Sczepanski, J. T. & Joyce, G. F. (2014) *Nature* 515: 440-442.
[3] He, C., Gallego, I., Laughlin, B., Grover, M.A. & Hud, N.V. (2017) *Nature Chemistry* 9: 318-324.