HIGH VISCOUSITY ENVIRONMENTS: A POSSIBLE SOLUTION FOR THE STRAND INHIBITION PROBLEM. I. Gállego[1,2], C. He[1,3], B. Laughlin[1,2], M. A. Grover[1,3] & N. V. Hud[1,2], [1]Center for Chemical Evolution, [2]School of Chemistry and Biochemistry (isaac.gallego@chemistry.gatech.edu; hud@gatech.edu), [3]School of Chemical & Biomolecular Engineering, Georgia Institute of Technology, Atlanta, GA, USA 30332

Nucleic acid replication in modern living systems relies on highly evolved proteins. The mechanism by which the first nucleic acids (or their predecessors) were replicated before the advent of coded proteins is unclear. While many researchers remain enthusiastic about the RNA world hypothesis [1], a major challenge to this theory is the identification of a simple system capable of nucleic acid replication without the aid of enzymes. Impressive progress has been made in the selection of RNA molecules that can act as progressive polymerases [2], but evolution towards such complex enzymes would have been accelerated if there was a geophysical process that facilitated nucleic acid replication before the emergence of ribozymes [3].

For replication systems that rely on non-enzymatic template-directed synthesis a formitable bottleneck is a phenomenon known as *strand inhibition* [4]—the thermodynamic and kinetic favorability of forming a long duplex prevents separation of the duplex strands for long enough to allow monomer/oligomer binding and ligation along the single stranded templates (Figure 1) [5, 6].

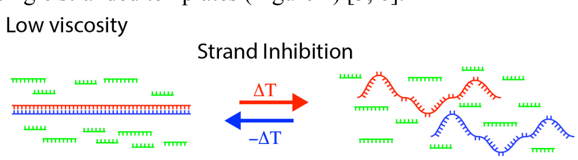

Figure 1. Schematic representation of the strand inhibition problem for long templates.

In a viscous environment, DNA mobility is slowed in a length-dependent manner, so that long DNA strands (such as template and product strands) can be kinetically trapped, slowing their annealing [7, 8]. Deep eutectic solvents (DES) are a new class of high viscosity solvents [9]. Recently, it has been demonstrated that nucleic acids can form a stable double helix in this anhydrous milieu, and that annealing is reversible with heating and cooling cycles [10].

In our model system we used DNA as an informational polymer. We show that DES can be used to control self-assembly kinetics of nucleic acids in a length-dependent manner. High viscosity is used as a means to control the annealing kinetics of a long template duplex after heating and cooling. Meanwhile, short oligomers can diffuse faster and bind to their complementary targets on the templates. Further ligation of the short oligonucleotides allow the production of the template copy, completing one cycle of replication. This process for template-directed synthesis, using a long duplex nucleic acid as a template, illustrates a possible solution to an important and unsolved problem in the origins of life field.

The miscibility with water and the tunability of DES, combined with thermal cycles, could be used to drive sustained rounds of nucleic acid replication. Such solvent systems might have been present on the prebiotic Earth, such as in tidal pools will dissolved organics that create a DES. During the day, heat would drive evaporation of water while denaturing long template strands, and at night the reduction of temperature would allow oligomers to bind the single stranded templates.

References:

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