STUDENT: Joshua Ballanco

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TITLE: A Model for the Evolution of Nucleotide Polymerase Directionality

THESIS ADVISOR: Marc Mansfield, Energy Dynamics Laboratory, Bingham Research Center

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ABSTRACT

In all known living organisms, every enzyme that synthesizes nucleic acid polymers does so by adding nucleotide 5'-triphosphates to the 3'-hydroxyl group of the growing chain. This results in the well known 5′ → 3′ directionality of all DNA and RNA Polymerases. The lack of any alternative mechanism, e.g. addition in a 3′ → 5′ direction, may indicate a very early founder effect in the evolution of life, or it may be the result of a selective pressure against such an alternative. In an attempt to determine whether the lack of an alternative polymerase directionality is the result of a founder effect or evolutionary selection, we have constructed a basic model of early polymerase evolution. This model is informed by the essential chemical properties of the nucleotide polymerization reaction. With this model, we are able to simulate the growth of organisms with polymerases that synthesize either 5′ → 3′ or 3′ → 5′ in isolation or in competition with each other. We have found that a competition between organisms with 5′ → 3′ polymerases and 3′ → 5′ polymerases only results in a evolutionarily stable strategy under certain conditions. Furthermore, we have found that mutations lead to a much clearer delineation between conditions that lead to a stable coexistence of these populations and conditions which ultimately lead to success for the 5′ → 3′ form. In addition to presenting a plausible explanation for the uniqueness of enzymatic polymerization reactions, we hope these results also provide an example of how whole organism evolution can be understood based on molecular details.